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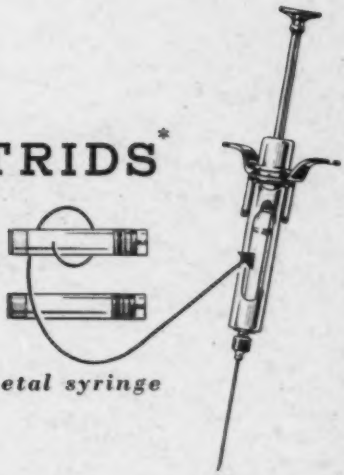

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The Journal of Pediatrics

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Original Communications

THE OCCURRENCE OF LYSOZYME IN THE CEREBROSPINAL FLUID AND SERUM OF INFANTS AND CHILDREN

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NEW HAVEN, CONN.

AS REPORTED originally by Fleming,[1] a bacteriolytic agent which he called lysozyme has been detected in many different biological fluids and tissues but not in cerebrospinal fluid. Lysozyme purified from egg white is apparently a basic polypeptide.[2] It functions as a depolymerase and a glucosidase when in the presence of a specific mucopolysaccharide derived from the lytically susceptible *Micrococcus lysodeikticus* or Sarcinae.[3] This paper describes investigations on the occurrence of lysozyme in the serum and cerebrospinal fluid of infants and children with and without acute infectious disease of the central nervous system. In this report the agent in the examined fluids which caused lysis of a well-studied strain of *M. lysodeikticus* is regarded as lysozyme.

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Aided by a grant from the James Hudson Brown Memorial Fund of the Yale University School of Medicine.

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MATERIALS AND METHODS

Specimens of serum and of cerebrospinal fluid were obtained from infants and children 2 months to 16 years of age who were admitted to the Pediatric Service of the Grace-New Haven Community Hospital. The samples were refrigerated immediately at 4° C. and were usually tested within twenty-four hours. When specimens were held for longer periods, they were stored in Lusteroid tubes at –70° C.

A modification of the method described by A. T. Wilson[4] was used to measure lysozyme. The culture of *M. lysodeikticus*, a descendant of Fleming's original strain, was obtained from the American Type Culture Collection.* The organism was cultivated on a tryptose phosphate agar slant (2 per cent agar) at 37° C. for forty-eight hours, and was then washed from the surface with 5.0 c.c. of M/30 phosphate buffer of pH 6.5. After thorough mixing, the bacterial suspension was diluted with additional phos-

*Dr. A. T. Wilson kindly provided the culture of *M. lysodeikticus*.

phate buffer to a standard density. An Evelyn-Malloy photoelectric colorimeter was employed. The 440 mm. filter was used and distilled water was the reference standard. Measurements were made in a large standard cuvette. The initial suspension was diluted until the galvanometer reading was 62.25. After preparation in this manner, the bacterial suspensions were used within two and one-half hours.

Each specimen of serum or cerebrospinal fluid was adjusted to pH 6.5 with 1 N.HCl or NaOH as needed. One drop of 1.0 per cent bromeresol purple was used as an indicator (pk = 6.3). Purulent fluids were cleared by centrifugation immediately after collection. Serial twofold dilutions of the cerebrospinal fluid or serum (0.5 c.c.) were made with M/30 phosphate buffer (0.5 c.c.). To each tube was then added 0.5 c.c. of the standardized suspension of *M. lysodeikticus*. The final dilutions of the fluids to be tested ranged from 1:4 to 1:1,024. Two control tubes were included with each series of tests. One contained 0.5 c.c. of phosphate buffer and 0.5 c.c. of the standard bacterial suspension—a lysozyme-free control. The second contained egg white, 0.5 c.c. of a 1:1,000 dilution in phosphate buffer, and 0.5 c.c. of the bacterial suspension—a lysozyme-containing control to demonstrate lysis of the bacteria.

The racks of tubes which contained the mixtures to be tested were placed in a water bath at 45° C. for two hours. At the end of this time, the tubes were examined against a constant source of light, and any lysis which had occurred was noted. The racks were then left in a refrigerator overnight at 4° C. On the following morning, the bottoms of the tubes were inspected for the presence or absence of a sedimented button of unlysed bacterial cells. This usually confirmed the findings of the earlier observation and was a satisfactory method of reading with respect to the reproducibility of results. The reciprocal of the highest final dilution of serum or cerebrospinal fluid which showed definite clearing of the standard suspension of *M. lysodeikticus* was taken to represent the number of units of lysozyme per cubic centimeters in the specimen.

PATIENTS

For the purpose of analysis the patients who were included in this study have been classified in three groups.

The first consisted of twenty infants and children who were examined at the hospital for various conditions other than infectious disease of the central nervous system. The results of tests with their cerebrospinal fluid were within the following limits: sugar 50 to 90 mg. per cent; total protein 15 to 40 mg. per cent; and leucocytes 0 to 10 per cubic millimeter. In the present study, the findings in this group have been considered as "normal."

In the second group were fifteen children with purulent bacterial meningitis. In each case one of the following microorganisms was cultivated from the cerebrospinal fluid: *Hemophilus influenzae* type b, pneumococcus type XIV, meningococcus, *Mycobacterium tuberculosis*, and *Staphylococcus aureus*.

The third group consisted of eleven patients who showed clinical and laboratory evidence of inflammatory disease of the central nervous system but whose cerebrospinal fluid yielded no growth when cultured on artificial

media. In this group were patients who had mumps or measles meningoencephalitis, one with polyneuritis, another with fever and convulsions of undetermined cause, and one with meningococcemia whose cerebrospinal fluid, although sterile, showed a lymphocytic pleocytosis without an increase in the protein content. Disease manifested by patients in the third group has been referred to as nonbacterial meningoencephalitis. It should be emphasized, however, that in this report the term has only a clinical connotation.

RESULTS

Lysozyme in Cerebrospinal Fluid.—Specimens of cerebrospinal fluid from twenty children who had no demonstrable infectious disease of the central nervous system were tested for lysozyme. Of this number, fifteen (75 per cent) had less than 4 units of lysozyme per cubic centimeters in samples of cerebrospinal fluid, and five (25 per cent) exhibited a titer of 4 units per cubic centimeters (Fig. 1*A*), which in this study appeared to be the maximal "normal" value.

High titers of lysozyme in cerebrospinal fluid were found in specimens from all fifteen patients with bacterial meningitis (Fig. 1*B*). Determinations made during the acute stage of illness ranged from 32 to 512 units per cubic centimeters. The highest titer was found in fluid from a child with meningitis caused by *Hemophilus influenzae* type b. In all patients who recovered, the lysozyme in the cerebrospinal fluid progressively diminished. This coincided with clinical evidence of improvement and paralleled the fall in spinal fluid protein and the restoration of spinal fluid sugar to a physiological level. The titers of cerebrospinal fluid lysozyme of less than 32 units per cubic centimeters which are shown in Fig. 1*B* were found in specimens which were obtained from patients with bacterial meningitis during convalescence.

Sixteen samples of cerebrospinal fluid from eleven patients with nonbacterial meningo-encephalitis were tested for the presence of lysozyme. Single specimens were obtained from each of seven patients during the acute stage of illness. The titer of lysozyme was 8 units per cubic centimeters in

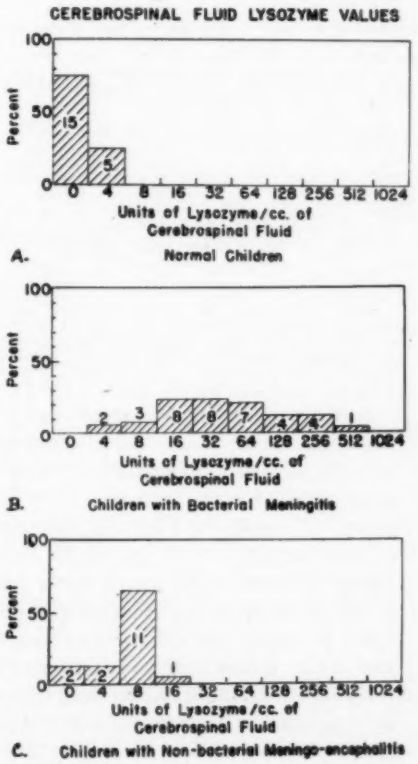

Fig. 1.—*A-C*, The height of each column represents the per cent of the total samples having such values. Numbers inside the columns represent number of samples showing these values.

six instances and 4 units in the other. From four patients, multiple samples of cerebrospinal fluid were obtained in series. The titer of lysozyme in specimens collected from them during the acute stage of illness was 8 units per cubic centimeters in three instances, and 16 units per cubic centimeters in the other. In the patients from whom serial samples of cerebrospinal fluid were obtained, a decrease in the titer of lysozyme to normal accompanied clinical improvement.

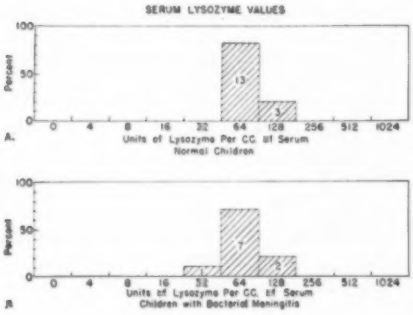

Fig. 2.—*A* and *B*, The height of each column represents the per cent of the total samples having such values. Numbers inside the columns represent number of samples showing these values.

Serum Lysozyme.—Sixteen specimens of serum from seven persons without apparent inflammatory disease were tested for the presence of lysozyme. As shown in Fig. 2 *A*, thirteen of these samples (81.2 per cent) were found to have a titer of 64 units per cubic centimeters, the remaining three (19.8 per cent) had a titer of 128 units per cubic centimeters. The results of tests for lysozyme with ten samples of serum from five children with bacterial meningitis are presented in Fig. 2 *B*. It can be seen that the distribution of these values coincided with the "normal" range. Four samples of serum were collected in series over a period of seven to ten days from each of three patients, one normal and two with bacterial meningitis. The titers obtained with these specimens were all within the normal range for serum and showed not more than a twofold variation from the mean.

Reproducibility of the Results.—Five samples of serum, two samples of cerebrospinal fluid, and one sample of a standard dilution (1:1,000) of egg white, each of which contained lysozyme, were subjected to duplicate and, in one instance, quadruplicate determinations of lysozyme on different days. The results varied consistently within the limits of one twofold dilution or one tube.

Relation Between Serum and Cerebrospinal Fluid Lysozyme.—From six patients with meningitis, specimens of serum and spinal fluid, which were collected concurrently, were tested for lysozyme. As shown in Fig. 3, the results reveal a wide range of values for cerebrospinal fluid, a narrow range for

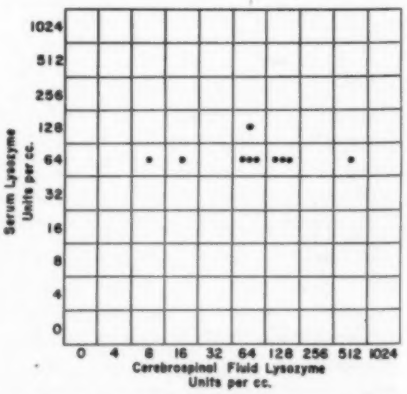

Fig. 3.—Comparison of cerebrospinal fluid and serum lysozyme titers. Each dot represents both values determined on samples drawn at the same time from one patient. Patients were acutely ill or convalescent from bacterial meningitis.

serum, and no indication of a direct quantitative relation between the two.

Source of Cerebrospinal Fluid Lysozyme.—Various correlations were attempted in an effort to infer the source of lysozyme in cerebrospinal fluid. In Fig. 4, the titer of lysozyme has been plotted against the measurement of total protein in each specimen of cerebrospinal fluid. A direct linear relation between these values is evident.

In Fig. 5, estimates of lysozyme and sugar in the same specimens of cerebrospinal fluid are similarly plotted. It can be seen that when the sugar was abnormally low, the titer of lysozyme was usually elevated, and that in general an inverse relation between these two values was apparent.

Fig. 6 shows the relation between lysozyme and the number of leucocytes in cerebrospinal fluid. It can be seen that in specimens with normal

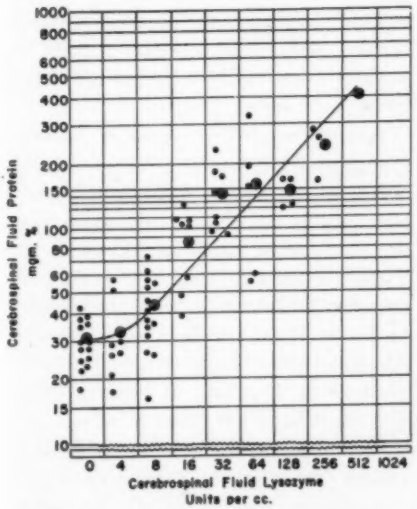

Fig. 4.—Correlation of cerebrospinal fluid lysozyme and cerebrospinal fluid protein values in normal patients, patients ill with bacterial meningitis, and patients ill with nonbacterial meningo-encephalitis. Dots represent individual values. Circled dots represent average values.

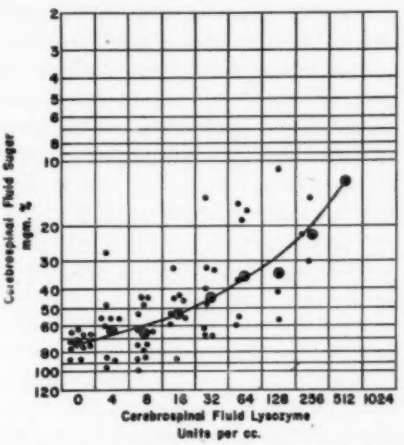

Fig. 5.—Correlation of cerebrospinal fluid lysozyme and cerebrospinal fluid sugar values in normal patients, patients ill with bacterial meningitis, and patients ill with nonbacterial meningo-encephalitis. Dots represent individual values. Circled dots represent average values.

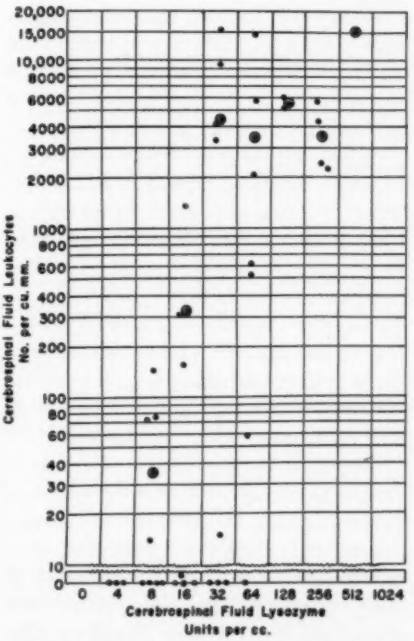

Fig. 6.—Correlation of cerebrospinal fluid lysozyme and cerebrospinal fluid leucocyte counts in patients with bacterial meningitis and with nonbacterial meningo-encephalitis. Dots represent individual values. Circled dots represent average values.

values for lysozyme no instances of pleocytosis were encountered, and that in specimens with elevated titers of lysozyme the leucocyte count was either normal or increased. With titers of lysozyme of 64 units or greater, the corresponding leucocyte count was almost invariably elevated. From these observations, it is apparent that lysozyme in cerebrospinal fluid may exceed the normal range even in the absence of pleocytosis. Furthermore, it is evident that a positive correlation exists between the titer of lysozyme and the total number of leucocytes per cubic centimeter of cerebrospinal fluid when this number is abnormally increased. The correlation was found to be statistically significant.*

It seemed possible that in cases of bacterial meningitis the microorganisms themselves might elaborate lysozyme into the cerebrospinal fluid. This possibility was, therefore, investigated. A strain of each of the following microorganisms which caused meningitis in some of the patients studied was grown for eighteen hours in an appropriate liquid medium: pneumococcus type XIV, *H. influenzae* type b, meningococcus, and *Staph. aureus*. A strain of *M. tuberculosis* was cultivated for seven days in Dubos' liquid medium. The cultures were, in each instance, cleared of bacteria by rapid centrifugation, and determinations of lysozyme were made with the supernatant fluid, as well as with an uninoculated batch of the respective media maintained otherwise under the same conditions. Lysozyme was detected in only one instance, the supernatant fluid from a culture of *Staph. aureus*, which contained 4 units of lysozyme per cubic centimeter. These findings did not entirely exclude the possibility that some microbial parasites might contribute to the occurrence of lysozyme in infected cerebrospinal fluid. They appeared to indicate, however, that lysozyme in the cerebrospinal fluid was derived mainly from the host.

*Dr. Max Woodbury, Statistician, Institute of Advanced Studies, Princeton University, confirmed this analysis.

DISCUSSION

Fleming, in his original report,[1] and later Fleming and Allison[5] and Thompson[6] noted that lysozyme was present in many organs, tissues, and fluids of the human body, including blood serum, pus, and leucocytes, but was not present in cerebrospinal fluid. Ridley[7] also found that leucocytes were a rich source of lysozyme. From observations made in the present study, it is apparent that lysozyme, although usually not detectable in the cerebrospinal fluid of normal children, is frequently present in cerebrospinal fluid during the course of inflammatory diseases involving the central nervous system, and, moreover, that it may be present even in the absence of leucocytes.

It has already been pointed out that lysozyme in cerebrospinal fluid is probably derived mainly from constituent elements of the host rather than from the pathogenic parasites. Possible intrinsic sources other than leucocytes include the meninges and transudates from the blood via the choroid plexus. The available data do not warrant conclusions as to which of these possible sources is the chief contributor.

The findings in two cases deserve special comment. One was a child with "infectious polyneuritis," the other had "encephalitis, etiology undetermined." Specimens of cerebrospinal fluid obtained from each of these pa-

tients during the acute stage of illness were sterile; they contained no leucocytes and a normal amount of protein and sugar. In both instances, however, the lysozyme titer was elevated to 8 units per cubic centimeter. These findings indicate that in certain instances the determination of lysozyme in cerebrospinal fluid may provide a more sensitive index of acute pathological changes in the central nervous system than measurements of protein, sugar, or leucocytes.

SUMMARY

Measurements of lysozyme were made upon specimens of blood serum and of cerebrospinal fluid from infants and children with and without acute infectious disease of the central nervous system. The technique employed depended upon the lysis of *M. lysideikticus*.

Lysozyme was invariably present in serum and showed little or no fluctuation in titer under different circumstances.

Lysozyme was usually not detectable in the cerebrospinal fluid of normal children but was found to be present during the course of inflammatory disease involving the central nervous system. The highest titers of lysozyme in cerebrospinal fluid were found in patients with purulent bacterial meningitis. Elevated titers were also encountered in the absence of pleocytosis.

The evidence indicated that lysozyme in cerebrospinal fluid is derived mainly from sources intrinsic to the host, and, in certain instances, may be a sensitive index of inflammatory disease involving the central nervous system.

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THE FEEDING OF PREMATURE INFANTS

The Value of High Caloric Diets in Reducing the Length of Hospital Stay

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INTRODUCTION

IT WAS noted by one of us (E. O. G.), at Sinai Hospital, that premature infants gained rapidly and did well when given a caloric intake considerably greater than that generally considered either necessary for optimum growth, or safe.

The practice in the Harriet Lane Home had been to feed premature infants according to a routine suggested by the studies of Levine and Gordon.[1, 2] The infants, after an initial period of starvation, are fed gradually increasing amounts until at the tenth to fourteenth day of life an intake of 120 calories per kilo of body weight per day is given. When the average daily weight gain of some of these infants was compared with those cared for at Sinai, a great discrepancy was noted, those at Sinai in some instances gaining almost twice as much as those at the Harriet Lane Home and being able to leave the hospital in little more than half the time. It was therefore decided to make comparative studies in an effort to establish these facts.

The present report consists of clinical observations made on three groups of patients. Groups A and B consist of infants, both Negro and white, cared for in the permature nursery unit of the Harriet Lane Home, The Johns Hopkins Hospital. The majority of these infants were born either at home or in other hospitals, and were transferred to the premature unit during the first forty-eight hours of life. In general, these infants came from families living under very poor socioeconomic conditions. Group C consists of infants born in Sinai Hospital and cared for in the premature nursery there. These infants were white and came from a considerably higher socioeconomic level of society.

The infants in Groups A and B, cared for in the Harriet Lane Nursery, include only well premature infants who were cared for by essentially the same techniques, and were given a formula consisting of partially skimmed milk (Alacta*) with 10 per cent dextrimaltose added to give a value of approximately one calorie per cubic centimeter (0.98 calorie per cubic centimeter). All feeding by mouth was withheld for twenty-four to forty-eight hours, and in the very small infants occasionally for as long as five days, then 5 per cent glucose solution was offered in small quantities for twelve to twenty-four hours before milk feedings were started. (Parenteral fluids were given where necessary to meet body fluid and electrolyte requirements.) The milk formula was then offered in small, but gradually increasing, amounts, allowing an increase of approximately ten calories per kilo of body weight per day until an intake of 120 to 130 calories per kilo of body weight per day was reached at 10 to

From the Department of Pediatrics, The Johns Hopkins University School of Medicine, The Johns Hopkins Hospital, and Sinai Hospital.

*Mead Johnson & Company.

14 days of age. The method of feeding, whether by gavage, medicine dropper, or nipple, was determined by the condition of the infant and its ability to suck and swallow. Supplementary vitamins A, C, and D were started on the fifth to seventh day of life. When the infant's weight reached approximately 2,200 grams, the formula was changed, in preparation for discharge from the hospital, to a mixture consisting of equal parts of evaporated milk and water, with 5 per cent carbohydrate added, giving a caloric value of 0.86 calorie per cubic centimeter of formula.

The forty-seven infants in Group A were admitted to the Harriet Lane Premature Nursery from June, 1947, to October, 1948. They were fed as previously outlined, and feedings were adjusted every two to three days so that an average intake of 120 to 130 calories per kilo of body weight per day was maintained.

The fifty-one infants in Group B were admitted to the Harriet Lane Premature Nursery between October, 1948, and May, 1949. They were treated in the same manner as the infants in Group A excepting that after two weeks of age the amount of formula offered was increased in accordance with the desires of the infant. No formula was forced upon an infant, but if the infant appeared hungry and willing to take more the amount was gradually increased. In this group, the infant taking the smallest amount averaged 121 calories per kilo of body weight per day while the one taking the largest amount averaged 195 calories per kilo of body weight per day.

The forty-seven infants in Group C were born and cared for at Sinai Hospital from July, 1947, to January, 1949. The routines used in the nursery differed only slightly from those used in the Harriet Lane Nursery. The Sinai infants were fed a formula of half skimmed milk with 7½ per cent dextrimaltose added, with a caloric value of 0.85 calories per cubic centimeter. Feedings were started twenty-four to forty-eight hours after birth and cautiously increased by 2 c.c. increments to the point of tolerance. In other respects, weighing, vitamins, bathing, and general nursing care was quite similar.

RESULTS AND DISCUSSION

Observations as to caloric intake per kilo of body weight, number and character of stools, regurgitation or vomiting were recorded on each infant's chart every day. The infants were weighed three times weekly. In computing this data the caloric intake for each infant from the time he reached 2 weeks of age until he reached 2,500 grams in weight or was discharged from the hospital was averaged, as were the number of bowel movements per day during the same period. The infants in each group, A, B, and C, were then separated, for the purposes of comparison, on a basis of birth weight, into three groups; those weighing 1,000 grams or less; those of 1,001 to 1,500 grams, and those weighing 1,501 to 2,000 grams. Six of the forty-seven infants in Group A were discharged from the hospital weighing between 2,400 and 2,500 grams; two were discharged weighing between 2,000 and 2,100 grams. Five of the fifty-one infants in Group B were discharged weighing between 2,070 and 2,380 grams. Seven of the forty-eight infants in Group C were discharged weighing between 2,225 and 2,395

TABLE I

WEIGHT AT BIRTH	†	NO. IN GROUP	SEX		RACE		AVERAGE WEIGHT AT BIRTH IN GRAMS	AVERAGE WEIGHT AT 2 WEEKS IN GRAMS	CALORIC INTAKE PER KILO PER DAY AFTER AGE 2 WEEKS*	WEIGHT GAIN IN GRAMS PER DAY AFTER AGE 2 WEEKS*	NO. BOWEL MOVEMENTS PER DAY AFTER AGE 2 WEEKS*	DAYS TAKEN TO REACH 2,500 GRAMS*
			M	F	W	N						
1,000 grams or less	A	4	2	2	1	3	932	937	125 119-133	16.8 13.3-19.5	3 2.6-3.7	99.5 89-115
	B	4	1	3	3	1	966	910	142 132-154	25.2 22.3-27.1	1.6 1.2-2.3	74.5 59-88
	C	1	1		1		971	978	175	26.5	4.2	66
1,001 to 1,500	A	21	11	10	14	7	1,244	1,235	125 115-136	18.4 12.7-26.1	2.3 1.2-3.4	76.8 60-108
	B	18	7	11	10	8	1,363	1,248	147.8 124-170	30 20.5-48	2.2 1.3-3.4	54 34-72
	C	20	5	15	20		1,288	1,408	191 153-246	30.7 21-45	3.9 2.5-8.2	49.7 30-64
1,501 to 2,000	A	22	7	15	13	9	1,684	1,775	123.9 110-137	21.3 15-28	2.1 1.0-3.1	46.5 28-63
	B	29	15	14	15	14	1,668	1,786	149.4 121-195	34.8 21.8-46	2.6 1.8-4.4	34.9 18-53
	C	26	10	16	26		1,736	1,907	190 160-233	40.8 24-63	4.1 2.8-6.1	28 18-41

*The upper figure represents the average value, the lower two figures the range.
†A-Infants cared for in the Harriet Lane Home receiving approximately 120 cals. per kilo of body weight per day.
B-Infants cared for in the Harriet Lane Home on a semidemand feeding regime.
C-Infants cared for at Sinai on a demand feeding regime.

grams. The number of days necessary to reach 2,500 grams was estimated on the basis of previous weight gain for each infant and added to the number of days spent in the hospital.

The results obtained may be seen in Table I. No diarrhea was encountered in any of the infants. One infant in Group A vomited three times; two infants in Group B vomited, one once, the other on two occasions. There was no significant increase in the number of stools per day in the two groups of infants cared for in the Harriet Lane Home.

It may be seen by referring to Table I that in each weight group there was a very significant rise in the average daily weight gain as the caloric intake was increased, and that there is a corresponding decrease in the number of days of hospitalization necessary to reach a satisfactory weight for discharge. It is of interest that there is a greater difference between the results obtained in the two groups of babies cared for in Harriet Lane than there is between those babies in Harriet Lane with a relatively high caloric intake (Group B) and those cared for at Sinai, who had an even higher caloric intake. It can readily be seen from Table I that the babies at Sinai at 2 weeks of age had not only regained their birth weight, but on the average surpassed this by a significant amount. This ultimately helped in reducing the total days of hospitalization. This can be explained by the fact that these babies received a higher caloric intake during the first two weeks of life than did those at the Harriet Lane Home. The babies at Sinai averaged 3.9 and 4.1 stools per day as compared with 2.2 and 2.1 for the babies in Harriet Lane Home, suggesting that a larger amount of the calories given was not utilized than was the case in Harriet Lane infants.

CONCLUSION

Although the results of this experiment do not prove that high caloric diet are necessarily the optimum diets for premature infants, it is demonstrated that high caloric feedings will increase the average daily weight gain and will reduce the infant's hospital stay significantly. Furthermore, that if the formula is increased cautiously and in accordance with the infant's desire, no ill effects are observed.

SUMMARY

Three groups of premature infants were compared as to their daily caloric intake, weight gain, and length of hospital stay.

1. Group A fed the usual 120 to 130 calories per kilo of body weight per day after 10 to 14 days of age showed the smallest weight gain and longest period of hospitalization.

2. Group B fed on a semidemand schedule after the second week of life showed a greater daily weight gain and required a correspondingly shorter period of hospitalization.

3. Group C fed on a demand schedule after the second day of life showed the greatest average daily weight gain and the shortest period of hospitalization.

The authors are indebted to Mrs. Norman Schaff for her help in assembling the data.

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TREATMENT OF HYPERTHYROIDISM WITH RADIOACTIVE IODINE

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ALTHOUGH internal radiation with radioactive iodine is being widely used in the treatment of hyperthyroidism in adults, there are few reports concerning the response of the juvenile thyroid to this relatively new therapeutic agent. The opportunity of using radioiodine in treating an 11-year-old Negro female with a diffuse toxic goiter and rheumatic heart disease was presented to us in 1948. The details of her response to internal radiation therapy are the subject of this report.

CASE REPORT

The patient, A. G., an 11-year-old Negro girl, was admitted to the St. Louis Children's Hospital on Oct. 12, 1948. She was the sixth of eleven siblings. The maternal grandmother is said to have had hypertension and a goiter. Parents and siblings were in good health.

The patient enjoyed good health until the age of 7½ years, at which time (February, 1945) she was admitted to the Homer G. Phillips Hospital of St. Louis. There a diagnosis of acute rheumatic fever with pericarditis and bronchopneumonia was made. At that time she received sulfathiazole for a period of five weeks. Her tonsils and adenoids were removed in June, 1945, and she was discharged from the hospital shortly afterward. Slight fullness of the neck in the region of the thyroid was noted during her hospital stay, but there were no other symptoms suggestive of thyroid dysfunction.

The patient was seen at regular intervals in the Cardiac Clinic at the St. Louis Children's Hospital until March, 1946. On a regime of restricted activity she gained weight satisfactorily and had no complaints. At the time of her last visit to the clinic, restlessness, tachycardia, and fibrillary movements of the protruded tongue were noted, and it was thought that she might be developing chorea.

However, she failed to return to the clinic and was not seen again until August, 1946, at which time she was admitted to the Homer G. Phillips Hospital, complaining of fever, vomiting, and pain in the abdomen and right hip region. Physical signs of rheumatic heart disease with mitral valvulitis were again noted. Symptomatic measures and bed rest resulted in relief of symptoms, although her pulse remained elevated (average 110). A fine tremor of the hands and tenderness and enlargement of the thyroid became evident, and a diagnosis of hyperthyroidism (diffuse toxic goiter) was made. The basal metabolic rate (calculated by means of the Wetzel Grid) was +36 per cent. Lugol's solution (5 drops three times daily) was given over a period of ten weeks, and she was kept in bed. The thyroid

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Radioiodine (I^{131}) was supplied by the Department of Radiology, Washington University School of Medicine.

gland decreased somewhat in size; she gained 5 pounds in weight, and her pulse fell to an average rate of 90 during this period. However, because the basal metabolic rate remained elevated (+38 per cent), prophylthiouracil therapy (75 mg. daily) was instituted in December, 1946. During the first six weeks of this new therapeutic regime her general condition failed to improve. Tachycardia and excessive perspiration became pronounced; the basal metabolic rate remained elevated (+31 per cent), and surgical thyroidectomy was seriously considered. Her general condition soon began to improve, however, and the drug was continued. By the time of discharge from the hospital in March, 1947, she had gained an additional 5 pounds in weight, and the basal metabolic rate was +27 per cent. Instructions to continue propylthiouracil were given.

The patient was next seen by us on Sept. 28, 1948, with classical signs of thyrotoxicosis. She had taken prophylthiouracil for only about a month following her discharge from the hospital eighteen months previously. She had no particular complaints until early in 1948 when "nervousness," excessive appetite, and hyperactivity developed. She began to lose weight; her eyes became prominent; sweating was profuse, and she complained of palpitation and tremor.

On admission to the St. Louis Children's Hospital on Oct. 12, 1948, at the age of 11 years, she appeared restless, apprehensive, and chronically ill. Her temperature was 37.8° C. (rectal), pulse 120, respirations 24, and blood pressure 160/74. Tremor of the hands and of the protruded tongue and slight exophthalmos without lid lag on downward gaze were present. The thyroid was diffusely enlarged, measuring 5 × 7 cm. in size, nontender, freely movable, and exhibited no bruit. The trachea was not displaced. The heart was overactive; a systolic thrill and murmur were noted in the apex region. The lymph nodes were not enlarged. The tip of the spleen could be felt beneath the left costal margin.

Laboratory studies revealed the following: Hemoglobin 11.8 Gm. per cent, red blood cell count 4,800,000 per c.mm., white blood cell count 6,200 per c.mm., with a differential count of 1 juvenile, 4 stabs, 59 segmentals, 33 lymphocytes, and 3 monocytes. Urinalysis was not abnormal, and the blood Kline and intradermal tuberculin tests were negative. The electrocardiogram was normal, and the sedimentation rate was 0.1 mm. per minute. A chest roentgenogram showed normal lung fields and cardiac silhouette except for slight fulness in the region of the pulmonary conus. The serum cholesterol was 159 mg. per cent.

Frequent determinations of the basal metabolic rate were made during the first ten days of hospitalization, and these ranged from +45 to +58 per cent. The patient's pulse and blood pressure remained elevated. She slept poorly and was extremely restless.

After it was ascertained by means of a tracer dose of I^{131} that the thyroid would collect radioiodine in a sufficient quantity to suggest a successful radiation effect, a therapeutic dose of radioiodine (5 mc., carrier-free) was administered by mouth in a single dose. The patient's subsequent course in respect to weight, basal metabolic rate, and serum cholesterol are depicted in Fig. 1.

Except for a gain in weight, there was little change in the patient's clinical course for the first four weeks. The temporary elevation in basal metabolic rate during the third week was not accompanied by any change in symptoms or signs of thyrotoxicosis. The basal metabolic rate dropped abruptly in the fifth week to +15 per cent, +23 per cent, and the pulse fell to an average value of 100. During the sixth week, a decrease in restlessness, exophthalmos, and in tremor of the extremities was noted, and the blood pressure fell to 135/85.

The patient was carefully observed for evidences of radiation sickness. Frequent blood counts were made, and a mild leucopenia (white blood cell

count 3,600 with 48 per cent segmented forms) and anemia (red blood cell count 3,850,000, hemoglobin 9.0 Gm. per cent) without thrombocytopenia occurred during the second week. The blood count then rose rapidly, and at the time of discharge from the hospital five weeks after therapy it was as follows: Hemoglobin 10.9 Gm. per cent, red blood cell count 5,900,000, white blood cell count 7,400 with a differential count of 5 stabs, 1 eosinophile, 62 segmentals, 30 lymphocytes, and 2 monocytes. Urinalyses revealed no abnormal findings, and serum calcium and phosphorus were normal.

By January, 1949, some ten weeks after radioiodine therapy, the patient exhibited no symptoms or signs of thyrotoxicosis, other than the persistence of mild hypertension and slight exophthalmos. The blood pressure did reach normal in July, 1949, and has remained normal (120/80) to date. The size of the thyroid gland gradually decreased until it measured approximately 3 × 4 cm., and it has remained that size. The gland became quite firm in consistency about two months after therapy but later softened, so that at the present writing its consistency is normal. Because of the reduction in basal metabolic rate to definitely subnormal values (lowest reading –35 per cent), the patient was given thyroid hormone orally, ½ gr. daily for six months. Despite the lowered metabolic rate, she evidenced no symptoms of hypothyroidism, and the serum cholesterol did not rise to abnormal heights.

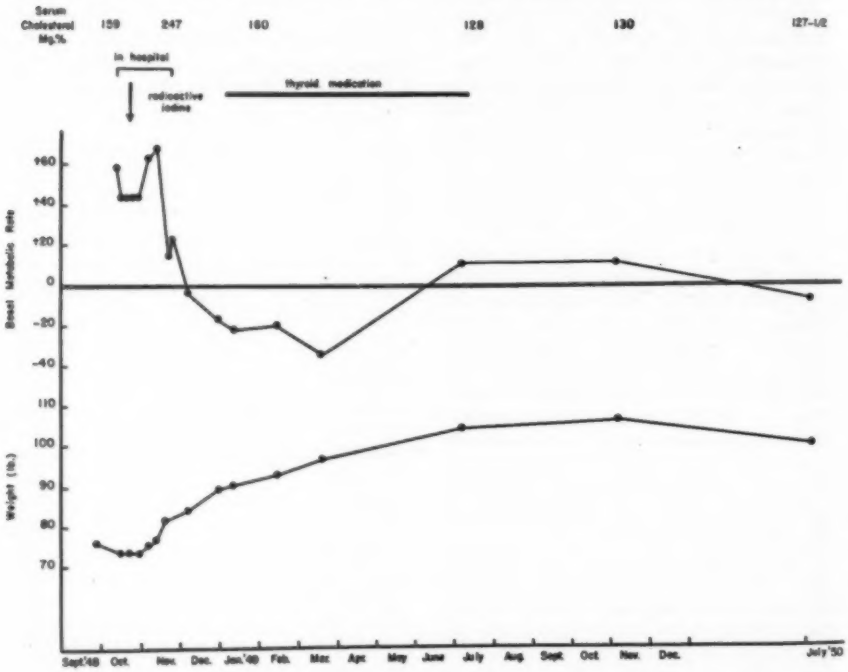

Fig. 1.—Clinical course of the patient as indicated by serum cholesterol, basal metabolic rate, and body weight.

By January, 1949, some ten weeks after radioiodine therapy, the patient exhibited no symptoms or signs of thyrotoxicosis, other than the persistence of mild hypertension and slight exophthalmos. The blood pressure did reach normal in July, 1949, and has remained normal (120/80) to date.

The patient's clinical course has been entirely satisfactory; she returned to school three months after therapy and has been able to engage in normal physical activity. Enlargement of the breasts was noted in July, 1949, and menarche occurred in Jan-

uary, 1950, at the age of 12 years, 2 months. Menses have been regular since. At the time of writing (July, 1950) the basal metabolic rate was −7 per cent, blood pressure 125/85, serum cholesterol 128 mg. per cent, and the thyroid uptake of radioiodine was within the normal range. The cardiac findings were unchanged, and investigation failed to reveal any cause for the loss of weight noted during the preceding eight months except that the dietary regime at home had been inadequate.

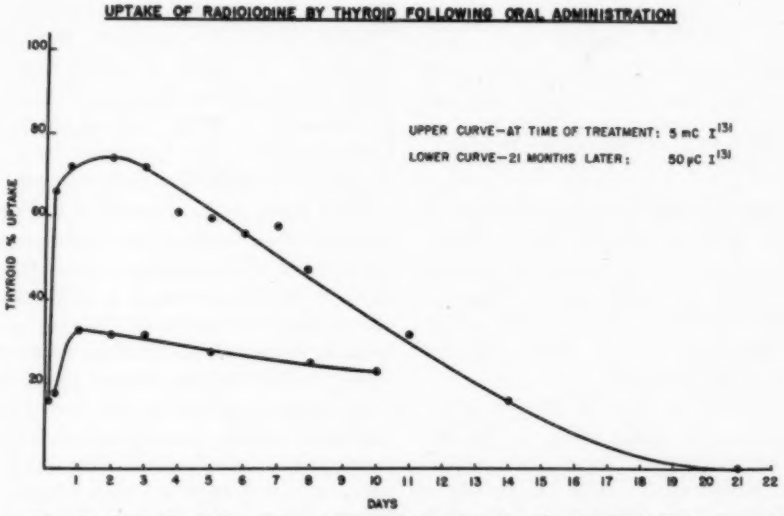
UPTAKE OF RADIOIODINE BY THYROID FOLLOWING ORAL ADMINISTRATION
UPPER CURVE—AT TIME OF TREATMENT: 5 mC I^{131}
LOWER CURVE—21 MONTHS LATER: 50 μC I^{131}
THYROID % UPTAKE
100
80
60
40
20
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22
DAYS

Fig. 2.—Thyroid uptake curves (corrected for decay) of radioiodine (I^{131}) measured at time of therapy (upper curve) and again twenty-one months later (lower curve). Carrier-free iodine was given on the first occasion, whereas 0.1 μg. of stable iodine was added to the tracer dose given later. Urinary excretion of radioiodine was inversely proportional to thyroid uptake: The forty-eight-hour excretion was 12 per cent of the administered dose on the first occasion and 55 per cent on the second.

For purposes of calculating the radiation dose received by the thyroid, these curves were redrawn with ordinate values in terms of microcuries of I^{131} per gram of tissue, the lower one being extrapolated to zero beyond the last day of observation see footnote, page 162).

Details of thyroid uptake of radioiodine during treatment and again twenty-one months later are illustrated in Fig. 2. Uptake was measured on the first occasion with a Lauritsen electroscope at a distance of 23 cm. from the neck, readings being taken before and after shielding the thyroid area with two inches of lead. On the second occasion, readings were taken with a lead shielded Geiger tube at a distance of 15 cm., using the thigh reading for background correction. The thyroid activity was compared to that of an aliquot of the administered radioiodine placed within a thin-walled glass cylinder measuring 3 cm. in diameter and 4 cm. in length. The upper curve is consistent with a diagnosis of hyperthyroidism, while the lower curve reveals an uptake within normal limits.[5, 6]

DISCUSSION

External radiation therapy has been used occasionally with success in juvenile hyperthyroidism. Ginsburg reported satisfactory results from the use of a collar containing radium needles in five adolescent girls.[1] The dosage employed ranged from 5,300 to 24,000 milligram-hours at a distance of 3 cm. from the thyroid gland; this roughly corresponds to a total dosage, at the gland surface, of 4,900 to 11,200 roentgens. Fear of skin burns and radia-

tion sickness, together with the fact that large doses must be employed, undoubtedly has tended to restrict the use of external radiation with either x-rays or radium in the treatment of this disease.

On the other hand, radioiodine delivers radiation directly to the thyroid gland, and other regions of the body receive a relatively small dose. Soley and Miller included two 9-year-olds and three 17-year-olds in their series of patients treated with radioactive iodine.[2] Dosage was given on the basis of estimated thyroid weight and ranged from 0.8 to 4 mc. The patients returned to normal in from two and one-half to six months, and their response to radioiodine therapy was judged to be satisfactory. Gordon and Albright included sixteen children 12 to 19 years of age in their recently reported series.[7] Response to therapy was considered satisfactory; details of dosage and subsequent clinical course for this particular age group were not given in their paper.

Radioactive iodine offers certain advantages over other types of therapy in thyrotoxicosis: It is administered as a single dose orally, a second or third dose being given at a later date if necessary, and, therefore, many patients can be treated as out-patients; acute toxic effects are infrequent, and most patients do not experience radiation sickness; the patient avoids the unpleasantness and risks attendant on surgical thyroidectomy and the need for close observation necessary during administration of one of the thiouracil derivatives; fortunately, the parathyroid glands are quite resistant to radiation effects, and tetany is not a therapeutic complication. These features account for the wide acceptance of radioiodine as the agent of choice in treating adult hyperthyroidism.

For the patient herein reported, radioiodine therapy seemed justified; she had failed to respond in a satisfactory manner to Lugol's solution; she had failed to cooperate to the degree necessary to insure success with propylthiouracil, and the risks of surgical thyroidectomy were increased by the presence of rheumatic heart disease.

Most authors, in discussing the use of radioiodine therapy, caution against its use in patients younger than middle age; presumably, fear of possible carcinogenic effects accounts for this attitude. Calculations of the radiation dose received by the thyroid gland of our patient according to accepted methods* results in a figure of 5,600 roentgens (roentgen equivalent physical), delivered over a period of about twenty days. Similar calculations of the radiation dose to the thyroid gland as a result of the tracer dose of I^{131} yield a figure of 38 roentgens. Radioiodine was first used in the treatment of patients some nine years ago,[3] and to date there have been no reports of

*This value is obtained by plotting the amount of radioiodine present in the thyroid gland, in terms of microcuries per gram of tissue, against time, calculating the area under this curve, and applying the formula (courtesy Mr. William B. Ittner):

$$1.33 \times 10^5 \times E \times 1.6 \times 10^{-6} \times \frac{1}{83} \int C\,(t)\,dt, \text{ where}$$

1.33 x 10^5 is the number of disintegrations per microcurie per hour,
E the average energy of the beta rays in million electron volts, (Mev),
1.6 $\times$ 10^{-6} the energy released (in ergs) per Mev.,
and C is the concentration of I^{131} in the thyroid gland in terms of microcuries per gram.
Divison by 83 converts energy in ergs to roentgens.

This gives the radiation dosage from beta ray activity, to which 10 per cent is added as an approximation of the gamma ray contribution.

a carcinoma developing in any patient so treated. Chapman and Evans in a recent review[4] emphasized the fact that radiation-induced cancer in human beings has always been the result of long-continued exposure. It is of interest to note that in our patient, although it is impossible to estimate the amount of radiation received by the ovaries as a result of treatment, menarche occurred at 12 years, 2 months of age, and menstrual periods are continuing normally.

The technical difficulties involved in the use of this new therapeutic agent limit its use at present to treatment centers possessing the necessary equipment to insure proper dosage to the patient and to protect medical and technical personnel from excessive radiation exposure. By virtue of the fact that radioiodine acts through destruction of thyroid tissue, overdosage may result in permanent hypothyroidism. We were fortunate in obtaining helpful advice from the Departments of Internal Medicine and Radiology whose radioiodine programs had been in progress for some time.

It is not our intent to suggest that radioactive iodine should be the treatment of choice in juvenile hyperthyroidism but rather to point out its usefulness in certain selected patients.

SUMMARY

1. A case of diffuse toxic goiter in an 11-year-old female is reported in which radioactive iodine therapy resulted in satisfactory relief of signs and symptoms of the disease.

2. Details of the patient's response to therapy are presented.

3. Radioiodine uptake curves of the thyroid gland obtained at the time of treatment and again twenty-one months later are presented.

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SOME OBSERVATIONS ON THE USE OF ADRENOCORTICOTROPIC HORMONE IN ATOPIC DERMATITIS IN INFANCY

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THERAPY of atopic eczematous lesions in infancy leaves much to be desired. In the common variety of infantile eczema, in which the lesions are largely limited to the face and surrounding area with occasional involvement of the flexor surfaces of the elbow and knee, temporary improvement is often obtained with local measures. When the lesions cover most or all of the body, as in the type designated by Hill as atopic erythroderma,[1] therapy rarely influences the course of the disease to a significant extent. It is because of this unsatisfactory experience that the results to be recorded here, which have been observed following administration of adrenocorticotropic hormone (ACTH*), seem significant.

In two therapeutic periods for each of three infants with generalized atopic eczema, remissions, which were complete or nearly so, were observed after short courses of ACTH administration. The clearing of the skin lesions and the abatement of the itching were so prompt in each instance and the recrudescence so consistent following cessation of therapy that there would appear to be no doubt of the therapeutic cause and effect.

From the Department of Pediatrics, Temple University School of Medicine, and St. Christopher's Hospital for Children.

This study was made possible in part by a gift from Mr. and Mrs. Harry Rifkin in memory of their son Myron.

*The Armour Laboratories.

CASE REPORT

CASE 1.—D.D., a male infant, 7½ months of age, was admitted to St. Christopher's Hospital for Children on May 23, 1950, with generalized atopic eczema. Although the rash had first appeared on the cheeks at three weeks of age, it was restricted to the face and flexor surfaces of the extremities for the first six months of life. During those months, there had been many formula changes, including evaporated and whole cow's milk, goat's milk, and Mullsoy, without any appreciable change in the skin lesions. Other foods that the infant had been given and which did not alter the skin lesions were cream of rice, barley cereal, carrots, applesauce, and peaches. When the infant was 6 months of age, the rash became generalized.

The infant was well developed and well nourished, weighing 20 pounds, 13½ ounces. With the exception of the palms of the hands, the soles of the feet, and a small part of the diaper area, the entire skin surface was involved. The skin was quite red, somewhat edematous, and there was some scaling of a seborrheic nature. There were lesions in all stages of development from the papule to the vesicle, some of which were covered with sticky, yellow crusts. Pruritis was intense, and there were many excoriations, but there did not appear to be an appreciable element of secondary infection.

The infant was placed on a pliofilm-covered mattress and was restrained to prevent scratching. The diet consisted of a Nutramigen formula, cream of rice, and the water-soluble vitamins in

the forms of ascorbic acid and Desynon. Mineral oil was used to cleanse the skin, and wet dressings of aluminum acetate solution were applied.

After one week on this regimen, there was less weeping, but the skin was still markedly erythematous, thickened, and scaling; there had been little real improvement. The pruritis was still intense.

On May 30, the administration of ACTH was begun with doses of 5 mg. at intervals of six hours. At the same time the entire diet was replaced with a formula of Lonalac (low sodium content) with 1 Gm. of potassium chloride added per day. Within twenty-four hours much of the erythema had subsided, and after seventy-two hours it had entirely disappeared. The itching appeared to be relieved within forty-eight hours, although some scratching persisted. After a six-day course of treatment, the skin was entirely clear of any eczematous lesions with the exception of some slight roughening.

ACTH was discontinued on June 5; the skin remained clear for several days, after which there was gradual recrudescence of the eczema. On June 14, another course of therapy was instituted in the same dosage and was continued for three days. Again, after twenty-four hours, the erythema had disappeared, and after the third day of treatment the skin appeared to be completely clear. When the ACTH was discontinued, coal tar ointment was applied in the hope that a relapse could be prevented. After several days, the erythema reappeared and was followed by return of some of the vesicular and papular lesions, but these were now limited to the face, chest, and flexor surfaces of the extremities.

On June 28, a new skin eruption was noted superimposed on the eczema, consisting of discrete vesicular lesions, varying in size from a few millimeters to 1 cm. There was a mild febrile response. There had been no known contact with a recently vaccinated person and no viral studies were carried out, but clinically the lesions appeared to be compatible with a diagnosis of Kaposi's varicelliform eruption. Aureomycin was administered, following which the lesions subsided, and the patient became afebrile within four days.

On July 6, when the infant was discharged to the care of his private pediatrician, there was eczematous involvement of the cheeks and flexor surfaces of the extremities. Six weeks after discharge from the hospital, the skin was relatively free of eczema with the exception of slight involvement of his legs; during this time there was no medication except pyribenzamine.

CASE 2.—J.C., a white female infant, 5½ months of age, was admitted to St. Christopher's Hospital for Children on June 5, 1950, with generalized atopic eczema. The eczema, which had been present since 6 weeks of age, had started on the cheeks and had remained localized until two months prior to admission when it had become generalized. Many dietary changes which included formulas of evaporated milk, whole milk, goat's milk, and Mullsoy, and a strict "eczema regimen" at home had failed to alter the progress of the eczema.

At the time of admission to the hospital, she was well developed and well nourished, weighing 12 pounds, 10½ ounces. There was a generalized weeping rash on an erythematous base with the skin being thickened and scaly. There were excoriations over most of the body as evidence of extensive scratching. She was placed on a pliofilm-covered mattress and was restrained to prevent scratching. Mineral oil was used to cleanse the skin and a 1:10,000 solution of Zephiran Chloride was used three times a day as a local application. The diet was limited to a Nutramigen formula, and phenobarbital was used as a sedative. Initially, there appeared to be some improvement of the eczema, but when on June 9 the formula was changed to Lonalac (low sodium content) with 1 Gm. of sodium chloride added, there was a flare-up of the skin lesions. On June 14, the administration of ACTH was

begun with doses of 5 mg. at intervals of six hours. The sodium chloride in the Lonalac formula was replaced with potassium chloride. Twenty-four hours later, there was dramatic improvement of the skin; most of the erythema had disappeared, and the lesions were drier. By the fourth day of therapy, the infant showed further improvement; she was more comfortable, had no erythema, and there were less scaling and thickening of the skin. The administration of ACTH was discontinued on June 18, and two days later there was recurrence of the skin lesions. On June 20, a second course of ACTH was started using the same dosage, and again there was improvement which was apparent within twenty-four hours. By June 23, after sixteen doses of ACTH, the skin looked better than at any time since admission. All of the erythema and weeping had disappeared, and the roughening and thickening had markedly improved. After the second course of ACTH, lanolin and Aquaphor ointment was applied locally in an attempt to maintain the improvement. Again in several days there was a remission.

On June 30, the infant was dismissed from the hospital to be followed in the out-patient department. In spite of various local treatments, antihistaminics, and a hypoallergenic milk, there has been no marked improvement.

CASE 3.—R.A., a white male child, 26 months of age, was admitted to St. Christopher's Hospital for Children on June 5, 1950. He had had eczema of short duration localized on the cheeks when he was 3 months of age, but was free of any skin lesion until November, 1949, at which time the flexor surfaces of his arms and legs became involved with eczematous lesions. Although there had been periods of partial remission and exacerbation, no etiological relationships had been noted, and in February, 1950, the rash became more generalized. There was marked pruritis during this time. About one week prior to admission, a mass developed behind the left ear.

At the time of admission, he weighed 24 pounds; the temperature was 101° F. In addition to large inguinal, axillary, and cervical nodes, there was a large, slightly fluctuant mass behind the left ear. The skin was covered with an exfoliative, seborrheic type of dermatitis which involved all parts of the body including the scalp, palms, and soles. There was no weeping except on the lower extremities which were covered with yellowish crusted lesions of an impetiginous nature. He was extremely unhappy and scratched continuously.

The child was placed on a pliofilm-covered mattress and was restrained from scratching. He was started on a full diet including whole milk, egg, cereal, meat, and orange juice. The skin was cleansed with mineral oil, and Aquaphor ointment was applied. Aureomycin and phenobarbital were given orally.

The temperature rose to 103° F within the next twenty-four hours, and the postauricular abscess became more fluctuant. This lesion was incised and drained, and the temperature returned to normal. After eleven days of aureomycin therapy, much of the adenopathy had subsided and all evidence of secondary infection had disappeared; however, the skin remained unchanged in other respects. The marked desquamation involving the entire skin surface persisted, and in spite of antihistaminics and heavy sedation with phenobarbital, the pruritis continued, and he was constantly irritable and uncomfortable.

On June 16, administration of ACTH in a dosage of 8 mg. at intervals of six hours was begun. Within twenty-four hours there was less desquamation and pruritis, and by June 20, all the desquamation had ceased, and, although no longer restrained, he did not scratch himself. For the first time since admission he was noted to smile. There was no change in the therapy or in the diet during the course of ACTH, with the exception of a gradual reduction in the amount of phenobarbital

administered until none was necessary. The skin remained completely clear for one week after the administration of ACTH was discontinued. There was slight itching, but not enough to warrant restraints. Thereafter, there was a gradual relapse, with roughening and thickening of the skin, followed by desquamation, erythema, and increasing pruritis. By July 31, the skin looked about the same as before treatment with ACTH.

At this time, ACTH was again administered in single daily doses of 10 mg. There was gradual improvement in the skin lesions, and by July 25, the skin was less erythematous and showed less scaling. Pruritis had subsided. Although the single daily dose of ACTH was continued, by July 29 there was definite evidence of exacerbation of the skin lesions and the pruritis was intense. On July 29, the dosage of ACTH was increased to 10 mg. at intervals of four hours. Within forty-eight hours there was no erythema or scaling of the skin, and the child again was comfortable. On July 21, the dosage of ACTH was reduced to 10 mg. at intervals of twelve hours. The improvement was maintained for forty-eight hours, and the dosage of ACTH was further reduced to 5 mg. at intervals of twelve hours. Within forty-eight hours, there was a slight but definite relapse manifested by erythema and roughening of the skin. Once again the dosage of ACTH was increased to 10 mg. at intervals of twelve hours. On August 4, in spite of the fact that this dosage had previously appeared to be adequate to control the eczematous lesions, this was not the case at this time. On August 11, the administration of ACTH was discontinued. Even though there had been a definite relapse during the time that small doses of ACTH were being administered, the child was in better condition than he had been prior to therapy with ACTH. On August 19, he was discharged weighing 27 pounds, 10 ounces, 3 pounds, 10 ounces more than at the time of admission and in a much improved physical state.

DISCUSSION

Though the offending allergens were not demonstrated in any of the three patients, there was little doubt but that each of them had an atopic form of generalized eczema. The skin manifestations of D.D. and J.C. were in a more acute stage of inflammation than were those of R.A. and exhibited more of a generalized erythema. In each of them widespread seborrhea was present, but in the case of R.A. it was extreme. It may be that the ages of the infants or the duration of the dermatitis may have in some way affected the skin responses, but except for the variations in the degree of erythema and seborrhea, whatever the reason, there were no marked differences in the clinical patterns.

The promptness of the subsidence of the skin lesions and of the itching following administration of ACTH in each of the six therapeutic periods was dramatic and left little doubt of the causal relationship. In view of the dangers of prolonged administration of ACTH, it would not seem justified to use this hormone as a therapeutic agent for eczema except as a temporary adjunct during periods of unusually severe activity of the eczematous lesions and perhaps during intercurrent localized or generalized infections. In such instances, ACTH may have a definite usefulness. To what extent the course of the varicelliform (Kaposi's) eruption in D.D. was influenced by the administration of ACTH cannot be stated. Perhaps the relative inactivity of the eczematous lesions at the time contributed to the mild course of the intercurrent skin infection. At any rate, the general manifestations were much less severe than is usually the case, and the course was less prolonged.

We have relatively little data concerning prolonged administration of small maintenance doses of ACTH, but the results with R.A. were not encouraging; Randolph[2] has had similar experience. Until further data are available, it cannot be stressed too strongly that continued administration should not be employed in general practice. It should be stated, however, that no evidences of untoward results attributable to the ACTH were noted during the relatively short periods of time that each infant received the hormone.

It may be that the most significant factor in the effect of ACTH on generalized atopic eczema in infants is the provision of a tool for the further study of this disease. It would appear that the statement of Hill,[3] that eczema in the young has as its basis an abnormality of constitution that cannot be changed, may require revision in view of the amassing evidence that the adrenal steroids are capable of altering the allergic tissue response which results from union of antigen and antibody.[4]

SUMMARY

It has been demonstrated that adrenocorticotropic hormone (ACTH) is effective in producing remissions in generalized atopic eczema (atopic erythroderma, Hill). The disease becomes reactivated following cessation of the hormonal therapy. The evidence available at the moment does not indicate that this agent has any place in the therapy of infantile eczema except possibly as a temporary adjunct during periods of unusual stress. Its use under such conditions is discussed. There was no evidence of untoward effects of ACTH on the infants treated for short periods of time in this study.

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A STUDY OF THE PROPHYLACTIC VALUE OF CHLOROQUINE IN CHILDREN

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IN SPITE of the large amount of available knowledge of malariology and mosquitology, the human plasmodia still kill thousands of people each year in Asia, Africa, and parts of Central and South America, and contribute to the retardation in mental and physical growth and development of millions of people in tropical climates around the globe. Even such temperate climates as the southern parts of the United States and the Mediterranean countries of Europe, Asia, and Africa do not entirely escape this scourge.

The exigencies of World War II served to reactivate interest in malaria control and prevention, and gave impetus to malaria studies on an unprecedented basis. During World War II, the American and British scientists operating under a coordinating committee of the Office of Scientific Research and Development, quite often released facts which were applicable to military field operation and contributed materially to the health and military efficiency of allied personnel operating in areas of high malaria endemicity. Through their efforts they contributed to the healthy return of millions of young men to civilian life, free of the devitalizing effect of malarial relapses. In spite of the excellent results of chemoprophylaxis and environmental control of malaria, related to the various emergency measures and use of the releases of an activated scientific group, many men returned from military service with plasmodia in their systems. These men are still having relapses.

During the greater part of the war, Atabrine was the drug of choice for malaria chemoprophylaxis. Its limitations and occasional contraindications were recognized in 1943, but it was not until SN-7618 (chloroquine) became available that a reasonable substitute was used. Several investigators hail chloroquine as superior to Atabrine as a malaria prophylactic. It is certainly easier to administer to large groups. One tablet (0.3 Gm.) taken by mouth at weekly intervals will prevent the disease as effectively as one tablet (0.1 Gm.) of Atabrine taken daily. They have the same defects in not acting on the sporozoite or extra-erytrocytic forms, and neither will prevent relapses in *Plasmodium vivax* and *Plasmodium malariae* infections.

One hiatus in the available knowledge of SN-7618 (chloroquine) as an effective chemoprophylactic is in the field of pediatrics. It is among children living in areas of high malaria endemicity that the disease is at its worst. While the adult may be the reservoir par excellence, the damages to the reticulo-endothelial system, the erythrocytes, the hemapoietic organs, and the central nervous system by the

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anoxemia resulting from the destruction of red blood corpuscles are more serious in the child; and, in fact, may so retard the normal, physical, and mental growth of the child until it will be impossible for him to become an economic or social asset to his country. The evil of the plasmodium is frequently attributed to destruction of the erythrocytes and pyrotoxin production. This is only part of the evil because the interference with the erythrocytic-maturing factor (E.M.F.) and the removal of available iron so essential to hemoglobin formation and function work a double hardship on tropical peoples living on a relatively low protein diet. The depression of the myeloblastic organs resulting in a neutropenia is another phase of chronic malaria which should be remembered.

Most of the studies on chloroquine do not include children. In some parts of the United States, children have been included in the studies, but there the investigators are dealing with a less fulminating type of malaria and in a practically controlled environment.

In Liberia, West Africa, where *Plasmodium falciparum* infection is the most prevalent of the malarias and where environmental control, except in the larger cities, is economically impractical, at present we are setting up a group of long-range observations on children. This article reports on 80 children between the ages of 2 years (18 pounds) and 18 years (140 pounds) in one group, and 100 children of similar age distribution in another group. These children live in two villages in the hinterland where a preliminary blood smear survey showed plasmodium in 42 per cent of the children. Histories on the first group of 80 children revealed that 48 per cent had one or more clinical attacks of malaria during the eight-month period prior to the beginning of the use of one (0.3 Gm.) chloroquine tablet per week, and 37 per cent of the second group of 100 cildren had one or more attacks of malaria during the twelve-month period prior to the use of a similar prophylactic dose of chloroquine. One tablet of chloroquine was given to each child at the same time each week, and no other type of malaria nor mosquito control was used.

At the end of the twenty-month period of the prophylaxis in one group and the twenty-four-month period of the prophylaxis in the other group, the following results were obtained:

4 per cent of the children had mild clinical attacks of malaria during the periods.

8 per cent of the children showed malarial parasites in their blood smears—all *P. falciparum* rings.

46 per cent of the children gave histories of one or more symptoms which could be reasonably attributed to taking the drug, but none were serious nor showed symptoms of *Lichen planus atypicus*. The symptoms were distributed as follows:

Slight headache	26%
Transient itching	16%
Dizziness or dyspnea	8%
Abdominal pain, "colic," or diarrhea	5%
Transient hematuria	1%
Nausea or vomiting	1%
Joint pains, increased muscular weakness or tremors	1%

These symptoms, when present, generally occurred during the first few weeks of therapy and were transient.

We, therefore, feel that 0.3 Gm. of chloroquine may be given weekly by mouth to children as young as 2 years of age (18 pounds) without serious danger and with good suppressible results. We, however, suggest that the initial dose be 0.15 Gm. in the smaller

children given in the evening after a heavy meal. Where dizziness occurs, the initial dose should be 0.15 Gm. taken at bedtime for the first few weeks. If no further symptoms develop, the dose may be increased to 0.3 Gm. within three weeks and then continued at that dose. A follow-up on the two cases of hematuria showed no persistent nephritis.

CONCLUSION

Chloroquine as a chemotherapeutic propylactic appears to be the most practical means of malaria control among the masses in tropical countries, where mosquito eradication, home screening, and the use of bed nets are economically impractical. Chloroquine prophylaxis is practical for children as young as 2 years (18 pounds).

AURICULAR SEPTAL DEFECTS IN CHILDREN

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THE auricular septal defect demands renewed attention since surgical closure is now entering the realm of possibility. Furthermore, a new factor in diagnosis has been introduced, namely, catheterization of the heart, which allows a more accurate and earlier recognition of the defect during life. In advanced cases in adult life, the clinical diagnosis has usually been possible, but in childhood, before the pulmonary artery and its branches show much change in size, the diagnosis has not been commonly made. In the past, our clinical knowledge has been based chiefly on a study of the histories of patients who have come to the post-mortem room. While this approach will continue to form the fundamental basis of our knowledge in auricular septal defects, several aspects may now be studied in childhood when the diagnosis can be verified by catheterization of the heart.

There have been excellent reviews of this subject in the past (White and McGinn,[1] Roesler,[2] Bedford and associates,[3] Taussig and collaborators[4]). All have emphasized the right ventricular hypertrophy, the grossly enlarged pulmonary artery and branches, and the frequently associated mitral valvular disease.

There has been considerable variation in the figures given regarding the frequency of auricular septal openings, for two reasons: first, because the frequent presence of a small unimportant patency of the foramen ovale in normal individuals, and second, because the auricular septal defect may be associated with some other far more important anomaly such as tricuspid atresia, pulmonary stenosis, etc., and its presence not recorded. We have not included atrioventricularis communis in this study since it always involves a combination of an auricular and ventricular septal defect, and produces a special clinical picture of its own which usually leads to a fatal termination in the first year of life. None of these three groups need concern us in a discussion of primary auricular septal defects. Our attention is directed chiefly to those whose major congenital anomaly is a significant opening between the auricles.

It has been stated repeatedly that a patent foramen ovale is the commonest congenital heart abnormality. It is certainly found with great frequency at a children's hospital where post mortems are often done in early life. However, a patent foramen ovale is normal in the first few months of life, and if it is functionally closed, although probe patent, in later life it should be considered normal also.

In a recent review of our post-mortem material and clinic cases from 1941 to 1948, the auricular septal defect was sixth in frequency in the clinic patients and thirteenth in frequency in the post-mortem studies. Both of these statements refer to its

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presence as a primary major defect. It is more common if its presence with other lesions is included.

In the 185 consecutive post-mortem cases showing congenital heart anomalies, there have been four with auricular septal defects where this was the major cardiac abnormality.

PRESENT STUDY

It is important to diagnose the condition as early as possible: first, because the physician may help the patient by management of his physical activity; second, because early diagnosis may become of considerable importance as surgical therapy improves and especially when it becomes a highly effective and safe procedure. With these points in mind, we have reviewed our clinic cases and find fourteen with evidence of an atrial septal defect confirmed by cardiac catheterization, and two other cases that seem to fit into the same group although we have not as yet had an opportunity to check them with cardiac catheter studies. A summary of the various findings in these fourteen proved cases was prepared in tabular form and the following is a review of these data.

The ages ranged from 1 year, 10 months up to 13 years with an average of 7.7 years. This group was considerably younger than most groups reported in the literature. There were eleven females and three males in the group. Several observers have reported a greater number of females with this defect but the preponderance is not usually so marked as we found it.

Three-quarters of our patients were thin but the other quarter were of an average physique without obesity. These findings are in keeping with the belief, frequently expressed in the literature, that these patients have a thin, emaciated appearance. However, we were interested to note that they were not always of this type.

The exercise tolerance was good in five, moderate in seven, and poor in two. We were frequently surprised to find an excellent exercise tolerance in a child that had considerable enlargement of the heart. As a general rule these children led normal lives so far as their physical activities were concerned.

There was a general absence of cyanosis. One exception was R. A. who developed transient heart failure and showed a minor degree of cyanosis of the lips which disappeared as the failure was relieved. The oxygen saturation of the femoral arteries lay between 87 and 95 per cent in the group studied.

It is of interest to determine the time at which the heart murmur was first noted because it gives us some indication of when a congenital heart defect was first suspected by the family doctor. These murmurs may have been audible at an earlier date but had not been mentioned to the mother by the examiner. In four cases the murmur was noted in the first year of life, in one it was noted in the second year, and in eight between 4 and 8 years of age. In one case the murmur was not noted until the child was 13 years of age. This, then, is one congenital heart defect which is not readily suspected in the neonatal period, and frequently the presence of an abnormality is not recognized until the child is of school age. It is worth emphasizing, however, that there were at least four patients who had sufficiently distinctive murmurs to make the family doc-

tor suspect an anomaly of the heart during the first year of life.

Nearly every child with an auricular septal defects has some increase in the force of the heartbeat. This was often best elicited by having him sit up and lean forward slightly. When the palm of the hand had been placed over the precordium one could appreciate the increased force of the heartbeat through the relatively thin chest wall.

A thrill was present in only one out of twelve cases of auricular septal defects. It was present in several cases reported by Bedford and associates[3], but they were in an older age group. In our experience it is rarely present in children.

All had murmurs up the left border of the sternum. In two-thirds the murmur was maximum in the first and second left interspaces, and one-third was maximum in the second and third left interspaces. Both the site and the quality of the murmur are important for diagnosis. The murmur is usually of moderate intensity and not as harsh and loud as in pulmonary stenosis. Occasionally, it may have a low-pitched quality suggesting a functional murmur rather than one associated with underlying pathology.

The presence of an accentuated pulmonary second sound is suggestive of an increased pressure in the pulmonary artery. The intensity of the pulmonary second sound is often best appreciated in a third left interspace in these children, i.e., a little below the site of maximum intensity of the murmur. Here the second sound may be clear-cut and accentuated when it is somewhat blurred up in the pulmonary area. It must be remembered that the pulmonary second sound is ordinarily greater than the aortic second sound in children. This must be taken into account when evaluating minor degrees of accentuation.

Of the fourteen children who were investigated by catheterization of the heart, all but one showed enlargement of the heart, two-thirds had moderate or grossly enlarged hearts. This finding is interesting in that these children looked so well and had led active lives in most instances. The enlargement appeared to be slowly progressive in several cases which is in keeping with what we know of the course of the disease and predicates the eventual outcome. It is perhaps noteworthy that one patient had no sign of cardiac enlargement. The measurements were well within the limits of normal.

The size and shape of the pulmonary trunk were checked by x-ray and fluoroscopy and it was found to be enlarged in every case. Sometimes we needed both anteroposterior and left anterior oblique views to verify the size of the pulmonary artery because in the anteroposterior view the whole left border appeared enlarged and straightened so that the pulmonary trunk did not appear as a separate bulge. However, in the left anterior oblique view, the aortic and pulmonary windows could be seen to be well nigh obliterated. Approximately 50 per cent showed the classical localized bulging of the pulmonary trunk in the anteroposterior view.

While the hilar shadows were increased in every case, not all showed expansile pulsation. Eleven of the fourteen showed this sign. In two, the pulsations could not be seen in the hilar shadows, and in one, the heart

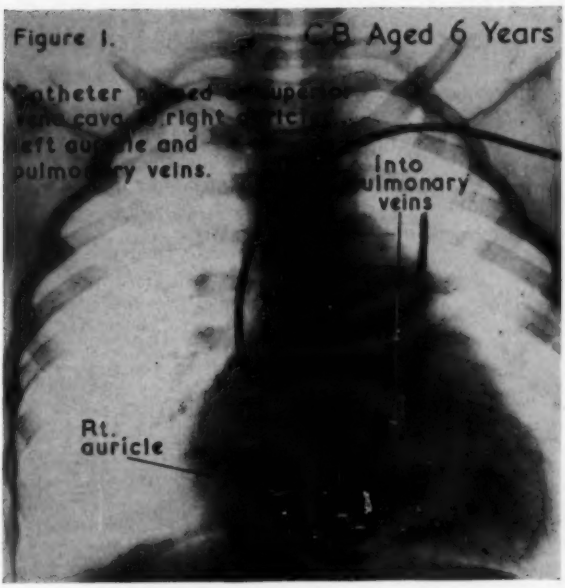
Figure 1.
C.B. Aged 6 Years
Into pulmonary veins
Rt. auricle

Fig. 1.

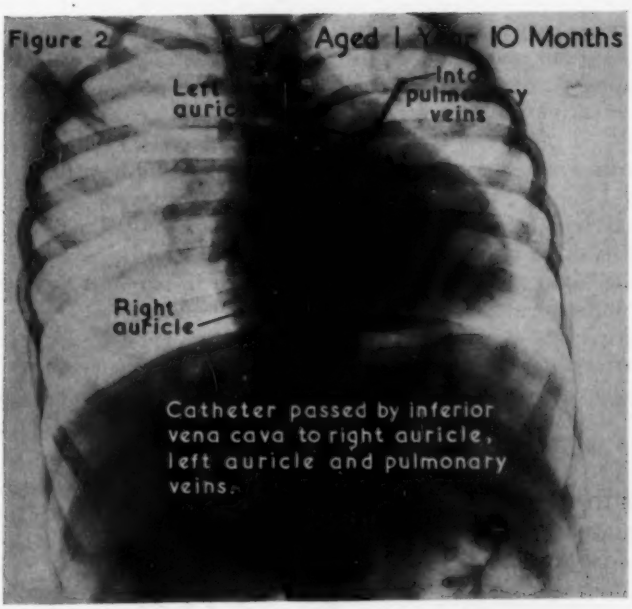
Figure 2
Aged 1 Year 10 Months
Left auricle
Into pulmonary veins
Right auricle
Catheter passed by inferior vena cava to right auricle, left auricle and pulmonary veins.

Fig. 2.

was so large that the hilar shadows were obscured and could not be seen. Expansile pulsation of the hilar shadows on the right is a most useful sign, because when it is obvious, it suggests increased pulmonary artery pressure and thus aids in diagnosis. Enlarged hilar shadows are common in children with respiratory infection, but in such cases there is no evidence of expansile pulsation. Furthermore, the shape of the heart in auricular septal defect is somewhat similar to that of rheumatic heart disease. Both conditions may have enlarged hilar shadows but the shadows do not pulsate in the rheumatic type.

A useful diagnostic point is the presence or absence of right axis deviation in the electrocardiogram. It was present in nine cases. There was no axis deviation in three cases and left axis deviation in two. The absence of right axis deviation does not rule out the diagnosis of auricular septal defect but its presence in association with the above-mentioned signs is of considerable help in arriving at a clinical diagnosis.

The cardiac catheterizations were performed using a No. 6 radiopaque cardiac catheter which was introduced into the left basilic vein just above the elbow, under local anesthesia. It was passed by the superior vena cava to the right auricle, right ventricle, and pulmonary artery. In five instances it was possible to pass the catheter through the defect into the left auricle and so on into the pulmonary veins (Figs. 1 and 2). The child was given a mild sedative before the procedure, and fluoroscopic control was used to follow the movements of the catheter.

The pressure in each chamber was recorded by a Hathaway Electrical Recording System. Earlier studies were made using a simple water manometer. We have found that the normal pressures in children are slightly lower than those obtained in adults.

A blood sample was taken from each chamber and its oxygen content determined by the Van Slyke method.

Anatomical proof of the presence of an auricular septal opening is obtained by passing the catheter into the left auricle. However, it is generally accepted that a difference in oxygen content of 2 vol. per cent or more between the blood in the superior vena cava and right auricle is usually found when a significant opening between the auricles exists (Cosby and Griffith,[6] Dexter[7]).

This minimum of 2 vol. per cent rise is evident in the cases presented, and in many, the auricular, ventricular, and pulmonary artery pressures are raised.

In 1947, Cohn[8] described an ingenious method of closing interauricular septal defects in dogs. In 1948, Murray[9] reported his work in attempting to close auricular septal defects in human subjects. At operation, silk sutures were passed through the plane of the auricular septum. These were drawn taut and tied in an effort to close or eliminate the opening between the auricles. One of our patients, on whom we had performed a catheterization to confirm the diagnosis of auricular septal defect, was operated on by Dr. Murray by this technique.

Since we have assembled a good deal of data before and after operation, she is included in this report. A heart murmur was first noted by the family doctor when she was 4 months of age, in 1940. Subsequent developement

was slow, and she was always backward compared with the other children. She had a poor appetite, appeared thin, and was easily tired. She had occasional pains in the legs but there was no illness resembling rheumatic fever. Because she was a weakly child she was not sent to school but instead she had a visiting teacher. In February, 1948, she was seen in the cardiac clinic of the Hospital for Sick Children and the clinical findings suggested a diagnosis of mitral insufficiency and auricular septal defect. In March, 1948, she was admitted to the hospital complaining of anorexia, tiredness, and breathlessness on exertion. She was found to be in early cardiac failure, and the liver was two-finger-breadths below the costal margin.

In August, 1948, an operation for closure of the auricular septal defect was performed by Dr. Gordon Murray.[9] She had a satisfactory convalescence from the operation and was sufficiently improved to attend school from October, 1948, until March, 1949. She did not go every day in the week and was off occasionally with colds, but she was able to pass her year examinations. In May, 1949, she again became tired and breathless on exertion. In July, 1949, she had an acute attack of breathlessness indicative of early cardiac failure, and she was put back on digoxin. The cardiac catheterization was repeated in October, 1949, and catheterization findings before and after operation are compared in Table I.

TABLE I. SUMMARY OF THE HISTORY AND FINDINGS IN OUR PATIENT R. A., AGED 10 YEARS

		CATHETERIZATION FINDINGS	
March 10, 1948	Oxygen content of	superior vena cava	11.0 vol. %
		right auricle	17.5 vol. %
		right ventricle No. 1	16.6 vol. %
Before operation		right ventricle No. 2	15.5 vol. %
		pulmonary artery	16.2 vol. %
		capacity	19.6 vol. %
	Operation August, 1948		
Sept. 21, 1949	Oxygen content	superior vena cava	9.0 vol. %
		right auricle	14.0 vol. %
After operation		right ventricle	14.3 vol. %
		pulmonary artery	14.6 vol. %
		capacity	17.8 vol. %
	Pressure in right auricle	Systolic 24 mm. Hg	
		Diastolic 0 mm. Hg	
	Pressure in right ventricle	Systolic 50 mm. Hg	
		Diastolic 0 mm. Hg	

Signs of failure disappeared with the use of digoxin. Cardiac catheterization was performed in March, 1948, which confirmed the diagnosis of auricular septal defect. Clinical examination at the same time revealed a mitral systolic murmur as well as a loud pulmonary systolic murmur. A faint early mitral diastolic murmur was heard at times at the apex suggesting mitral stenosis.

There is a rise in oxygen content of 6.5 vol. per cent going from the superior vena cava into the right auricle in the cardiac catheter study before operation. After operation the rise in oxygen content was 5 vol. per cent.

The intracardiac pressure curve before operation was obtained with a temporary apparatus that was not accurate and therefore the figures are not suitable for comparison. However, follow-

ing operation, systolic pressure in the right auricle and right ventricle was about twice as high as normal. The shape of the pressure curve in the right ventricle showed a deep double spike at the height of systole followed by a lower curve, falling away to diastole. It resembled that found in certain other patients with auricular septal defects.

murmur of moderate intensity in the first to third left interspaces. The murmur is not accompanied by a thrill but is usually associated with an accentuated second heart sound down the left border of the sternum. The electrocardiogram usually shows right axis deviation and under the fluoroscope one sees a slight to moderately

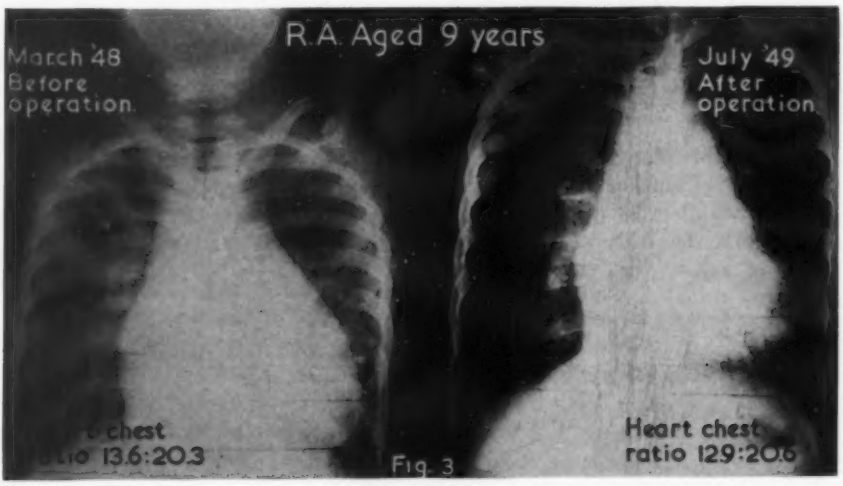

Fig. 3.

An x-ray taken in March, 1948, and one taken in July, 1949, are shown in Fig. 3. There seems to be a slight generalized decrease in heart size. The right auricle in particular appears smaller and the left border and apex not so full.

DISCUSSION

A review of our clinical findings in children with auricular septal defects suggests that there is a common pattern that will frequently permit one to make a presumptive diagnosis on physical examination alone. The typical patient is a somewhat thin, 7-year-old girl who has an increase in the force of her heartbeat, and a systolic

enlarged heart with increased and pulsating hilar shadows. The pulmonary trunk is enlarged, sometimes bulging out in an emphatic murmur. The catheterization of the heart reveals an increase in the oxygen content of the blood on passing into the right auricle from the superior vena cava of at least 2 vol. per cent. A close approximation of this pattern was found in most of our cases and allowed us to suspect the diagnosis at the initial clinical examination in all but two or three children.

There are a number of cardiac anomalies that may simulate a defect of the auricular septum. Patent ductus arteriosus, pulmonary stenosis, idio-

pathic dilatation of the pulmonary artery are three that give murmurs in the same area. The patent ductus can usually be differentiated by its continuous murmur, but occasionally this may be limited to systole, and cardiac catheterization studies are required to establish the correct diagnosis. Pulmonary stenosis and idiopathic dilatation do not show pulsating hilar shadows.

Pulmonary vascular disease and pulmonary disease may eventually produce some enlargement of the pulmonary artery trunk, but it is not marked, Neither of these conditions is associated with pulsating hilar shadows.

A ventricular septal defect produces a murmur that is usually best heard in the fourth left interspace. There is little or no cardiac enlargement as a rule and rarely does one find pulsating hilar shadows. In young babies, with a large defect, there may be a greatly dilated pulmonary trunk. This is especially true if there is an associated over-riding of the aorta (Eisenmenger's complex). In such instances it may be very difficult to make a correct diagnosis on clinical grounds and the cardiac catheter may be needed to solve the problem. Our experience with the cardiac catheter, however, leads us to believe that one does not usually confuse the Eisenmenger's complex with auricular septal defect, when examining the patient clinically. The type and location of the murmur in Eisenmenger's complex have been an important guide to us since it is usually found in the third and fourth left interspaces and is loud and harsh and frequently accompanied by a thrill. This is not the usual picture in auricular septal defect.

Perhaps the most difficult differentiation to make is between patients with a mitral insufficiency and those with auricular septal defects. A mitral diastolic murmur will usually allow one to make a diagnosis of mitral stenosis, with confidence. A systolic murmur at the apex may sometimes be due to tricuspid insufficiency from the great dilatation of that valve, or occasionally from the enlargement of the left ventricle. However, a mitral systolic murmur transmitted to the axilla should make one suspicious of mitral disease. A good guide in differentiating mitral stenosis and auricular septal defect is fluoroscopic examination since one finds pulsating hilar shadows in auricular septal defects and simply congested shadows in cases with plain mitral insufficiency or stenosis.

The presence of an auricular septal defect may be shown by cardiac catheterization but the procedure helps little in the diagnosis of mitral valvular disease. The entry of a pulmonary vein or veins into the superior vena cava gives an abnormally high oxygen content of blood from that site, and thus permits an accurate diagnosis of the condition. Pulmonary veins communicating with the right auricle produce oxygen content figures that are similar to those found in auricular septal defect. The latter may be distinguished only if the catheter enters the left auricle, and the former if one of the pulmonary veins is entered from the right auricle. Fortunately, pulmonary veins into the right auricle is a rare congenital anomaly and has only been encountered twice in the past twenty years at the Hospital for Sick Children.

In 1934, Roesler[2] summarized the available literature up to that time on auricular septal defects, and noted that the average length of life was 36 years of age in those who had died of the disease. Since then Bedford,[3] in 1940, and Cosby,[6] in 1949, have reported groups either seen in their clinic or at the post-mortem table. The time of death is usually between 30 and 50 years of age but occasionally individual patients have lived to be 80. At the other end of the scale are those in our own series who died at a few months of age with both mitral disease and a septal defect. The average length of life in the group reported by Cosby in 1949, 49 years of age, is thirteen to fourteen years longer than the average length of life in the post-mortem groups reported by either Bedford or Roesler. The chief difference between the post-mortem group reported by Cosby and those of Bedford and Roesler was the absence of mitral stenosis. Bedford found mitral stenosis in 40 per cent of his post-mortem cases, and Roesler 50 per cent. At the same time it should be pointed out that Roesler found no significant difference in length of life in those without mitral disease when compared with those with the combined defect.

The absence of mitral stenosis in Cosby's post-mortem group may be a reflection of the apparent drop in mortality from rheumatic heart disease during the last twenty years, or it may be looked upon as support for the belief that there is a lower incidence of rheumatic heart disease in California than in more northern climates. In any event, when considering the risks and possible benefits of surgery in auricular septal defects, it is extremely important to realize that at least one observer found an average age of 49 years.

A further consideration is that these patients go through a period of ten to twenty years of progressive slight impairment of their exercise tolerance, which preceded a final interval of incapacitation from heart failure leading to death (Bedford). They nearly all die of heart failure or complications associated with it, and as is noted in all series, bacterial endocarditis is a rare finding in any one of these cases.

In contemplating surgery for these children, one should clearly divide them into two groups, those who have associated mitral disease and those who have not. There is considerable evidence to indicate that the presence of an auricular septal defect is of benefit in cases of mitral stenosis. This has been supported recently by the work of Bland and Sweet.[10] They have reported five patients with mitral stenosis, four of whom were improved by having one of the pulmonary veins anastomosed to the great azygos vein, thus producing the same sort of shunt that occurs in an auricular septal defect. Such operative therapy appears to be particularly valuable in cases of mitral stenosis that have recurring bouts of pulmonary edema. Dyspneic attacks, while at rest, are diminished or eliminated, and their exercise tolerance is improved by the production of this abnormal shunt. Such experience suggests that even with improved techniques it may prove unwise to correct an auricular septal defect when mitral stenosis is present also.

In 1948, Murray[9] reported a method of treating auricular septal defects

surgically. One of our patients was treated by him in this manner with results detailed above. The possible benefits of such therapy were evaluated by three methods. First, the exercise tolerance showed a moderate temporary improvement following operation, which was sustained for six to eight months. Her exercise tolerance, at the time of writing, is the same as before operation. Second, the catheterization showed an oxygen content of various chambers that did not indicate much improvement as a result of operation. The shunt from left auricle into right auricle appeared to be of the same order in the studies after operation as before. We could not compare pressures because they were carried out by a different method before and after operation. Finally, the x-ray allowed further comparison. There was a definite decrease in the measurements from a transverse diameter of 11.8 to 10.8 cm. following surgical intervention. Furthermore, the shadow showed a generalized decrease in size as is evident in the two radiographs produced above. Murray reports a notable decrease in the size of the right auricle at the time of operation in such cases, when the sutures are drawn tight and tied. This may account for the difference in cardiac measurements. However, the generalized decrease in size suggests that there may be beneficial effect suggesting more than mere mechanical alteration in the shape of the right auricle.

In evaluating the exercise tolerance and catheter findings one should also bear in mind that there may have been some reduction in the flow from the left to right following operation, but that continued movements of the heart over several months may have enlarged any opening remaining between the auricles and returned the flow to its previous proportions.

The technique described by Murray would appear to carry less risk than that reported by Cohn.[8] It is possible that the method used in our patient, who had mitral disease as well, might be more effective in those with no such mitral complications. A defective mitral valve increases the pressure in the left auricle and forces a larger amount of blood through the septal defect. The operation might be expected to control the flow more efficiently and maintain such control better if the defect between the auricles was not complicated by the mitral lesion.

Roesler's group of sixty-one cases was the only series that permitted any approach to the problem of the effect of size of the auricular septal opening on enlargement of the heart. He concluded, on somewhat limited data, that those with small septal defects (1 to 2 cm. in diameter) had smaller hearts than those with larger defects. However, there were patients who had grossly enlarged hearts with defects 1 to 2 cm. in diameter. This is important surgically since it points out the necessity of completely or almost completely closing the opening between the two auricles. Whether this can be done by a procedure carried on from outside the heart, or whether it will prove necessary to open the auricle to achieve successful closure, is a matter requiring further study.

The pressure differential between the auricles bears on the problem. There are several reasons for the slightly higher pressure generally found in the left auricle. Cournand[11] attributes it

to the smaller capacity and distensibility of the left auricle and pulmonary veins, and the effects of left ventricle activity on the volume and tension in the left auricle. Hull[12] feels that the larger tricuspid valve opening and the ease with which the right ventricle can be filled, as opposed to the left, diminishes the resistance to blood flow and thus lowers the pressure in the right auricle compared with the left auricle. He points out that once the interatrial shunt is instituted it leads to an increase in the capacity of the right auricle, tricuspid valve, right ventricle, and pulmonary artery, so that the shunt tends to increase gradually over the years.

From the surgical standpoint it becomes most important, as the disease progresses, that any surgical technique must adequately close the opening since the tendency for the shunt to continue will be great for some time. Even a small opening may allow a considerable shunt of blood, especially if a notable pressure differential between the auricles exists.

Since the right auricle is greatly enlarged as a result of the septal defect, it should not be of much concern to the surgeon if he reduces its size considerably during the course of the operation. If Hull's thesis is correct, a reduction in capacity of the right auricle, tricuspid valve, and right ventricle would tend to dimish the pressure differential between the auricles.

SUMMARY

The auricular septal defect is the sixth commonest congenital abnormality of the heart encountered in the cardiac out-patient clinic of the Hospital for Sick Children, Toronto. In the past, proof of the lesion has only been possible at post mortem, but now cardiac catheterization provides a method of diagnosis during life. A review of our children with auricular septal defect, proved by catheterization, suggests that a common pattern of signs exists in which a fairly accurate diagnosis can be made on clinical findings alone. The typical picture is a somewhat thin 7-year-old girl who has increased force of her heartbeat and a systolic murmur of moderate intensity in the first to third left interspaces; the murmur is not accompanied by a thrill but is usually associated with an accentuated pulmonary second sound down the left border of the sternum. The electrocardiogram usually shows right axis deviation, and under the fluoroscope one sees a slight to moderately enlarged heart with increased and pulsating hilar shadows, and the pulmonary trunk is usually bulging.

The importance of the accurate diagnosis of auricular septal defects lies in the guide thereby provided to the proper management of physical activity in the patient, and also in the consideration of cardiac surgery to correct the defect.

Details of a patient with auricular septal defect, treated by a new surgical technique, are presented. The evidence for postoperative improvement is discussed.

It is concluded that the optimum surgical correction of an auricular septal defect should eliminate the shunt between the auricles and return the heart size and exercise tolerance to normal. This will be difficult to achieve by present techniques, but enough has been done to suggest that the problem is not insuperable.

Untreated, these patients survive for approximately two-thirds of the nor-

mal span of life. This in itself warrants continued efforts to produce a form of therapy that will prevent the early onset of failure and allow these people to live a normal life span.

The authors wish to express their appreciation for the skilled assistance of Mrs. B. Thompson, R.N., and Mrs. J. MacDougall, R.N., in carrying out the cardiac catheterizations reported in this study.

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TRAUMATIC PERIOSTITIS IN YOUNG CHILDREN

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A COMMON pediatric occurrence, the "acute limping leg" of early childhood, has received little previous emphasis in medical publications. Often in these cases a traumatic periostitis of the tibia or femur is present, and is the result of some trivial, indirect injury associated with the daily activity of the child. A morbidity of office practice, traumatic periostitis does not respond to any manipulative procedure such as produces the dramatic recovery in subluxation of the radial head.[1]

The usual story is one of ordinary childhood injury, such as twisting the leg in falling, doing the "split" accidentally, or even following passive exercises for some orthopedic defect. Direct trauma to the leg is not a factor. The usual age of the child is between 1 and 2 years, though the condition occurs in the newborn infant, and one of our cases was a girl of 5 years.

Following injury, the child cries when the leg is palpated, and either refuses to place weight upon the leg, or limps with the traumatized member. There is tenderness and sometimes a sense of fullness along the tibia, but rarely is there appreciable soft tissue swelling. The child shows no sign of illness, eat normally, and is obviously well except for the involved extremity.

X-rays at the time of, or shortly following, the injury are invariably negative for fracture or other bone pathology, and the injury is considered to be a "sprain." Several days to a week later the child again begins to walk, limps for a varying period (usually for another week), and then recovers without incident. The experienced pediatrician soon learns to dispense with the initial negative x-ray, makes an accurate prognosis to the mother, and suggests radiography at a later date if recovery fails to ensue. Since the child inevitably does improve shortly, the delayed roentgenogram is seldom obtained.

If, however, a subsequent roentgenogram is taken at, or following, the time of recovery (some seven to ten days after injury), there will frequently be found evidence of an ossifying periosteal reaction which persists for many weeks, and which resolves completely in perhaps three or four months. No lamellation is noted, and the bony cortex shows no change. Most often it is the tibia which is involved, but occasionally the same pathology is seen in the femur. We have yet to recognize a case in the upper extremity, although the occurrence of the condition in a humerus of a newborn infant has been reported.

No treatment is necessary or indicated.

It is not difficult to speculate on the origin of this delayed periosteal reaction. Because the history of injury is almost always definite, and because the periosteum of children is known

From The Western Montana Clinic.

to be very readily dissectible from the bone, it can be postulated that a small subperiosteal hemorrhage is the precipitating factor in the disability. Mineral deposition by the separated periosteum, proceeding at a rate which parallels closely the development of the delayed radiographic periosteal reaction in healing scurvy,[2] then gives rise to the positive x-ray signs. An analogous situation is the prevalent subperiosteal hemorrhage called "cephalhematoma" in the newborn infant.

Many different pathologies may be implicated by the limping leg of a child. In the toddlers we have often been concerned by the possibility of congenital dislocation of the hip, even though the limp of hip-joint dysplasia is more insidious in its onset. The older children sometimes suggest the possibility of aseptic necrosis, with Perthes' and Koehler's diseases most probable, but here again the sudden onset of traumatic periostitis is absent. X-rays which include the hip joints and the tarsal bones should provide the answer. Atypical poliomyelitis must also be entertained as a diagnosis, as should greenstick fracture, with its profuse periosteal reaction.

For academic completeness, a wide range of periostitides might likewise be considered in the differential diagnosis, but most of these conditions may be brushed aside clinically with little more than the recognition of their existence. Obviously, there is no correlation between traumatic periostitis and either scurvy or syphilis; all of our patients have had an adequate vitamin C intake, the x-rays have revealed neither syphilitic nor scorbutic signs, and syphilitic stigmas have been uniformly absent. Rickets may be excluded with similar reasoning. Likewise, there are no systemic manifestations (i.e., fever and irritability) to suggest a relationship to the infantile cortical hyperostoses described by Caffey and by Smyth,[3] and the short, benign course of a localized traumatic periostitis serves well to differentiate it from the more generalized periosteal proliferations of the Caffey-Smyth syndrome. Hypervitaminosis A[4, 16] shows a striking resemblance radiographically to infantile cortical hyperostoses, but here again the systemic display of anorexia, weight loss, fever, rash, and extreme irritability serve to distinguish vitamin A overdosage from periostitis due to injury. So, too, the local heat and systemic reaction to an acute or subacute osteomyelitis makes this condition unlikely to be confused with a traumatic periosteal stripping. Finally, the localized, nodular type of periostitis associated with direct trauma (say to the medial tibial surface in athletes) is quite unlike the smooth and diffuse periosteal reaction of indirect trauma.

Radiographically, pseudoperiostitis[5] and double cortical contours[6] must be considered: pseudoperiostitis is often found on the concave side of the metaphysis of bones where the shaft curves into the epiphysis. Usually associated with arthritic disturbances or persistent localized swelling in adults, it may be confused with a genuine ossifying periostitis.

Glaser describes the double cortical contour in normal infants thus: "The surfaces of the long bones were frequently outlined by a double contour which gave the impression of periosteal thickening or elevation and/or cortical hypertrophy. These lines may

be present on all 4 bones of the distal parts of the extremities or on only 1 or more. . . . In the largest number of cases this double contour was observed for the first time during the third or fourth month. . . (and) began to be less frequently visible around the seventh and eighth months of life. . . . This phenomenon may be misinterpreted as a sign of a pathological process."

Many other bizarre but evidently unrelated types of periosteal reaction have been described. In "march foot"[7] there is a traumatic periostitis of the middle metatarsals, but this reaction is associated with fracture, and radiographic signs are delayed for about eight weeks after the onset of symptoms. March foot is the commonest example of a "creeping" or "fatigue fracture,"[8] i.e., a fracture occurring without an obvious single trauma, but one which develops as a result of rhythmically repeated mechanical insults. In the production of such a fracture four stages have been described: (1) periosteal neuralgia (stress pain); (2) ossifying or overload periostitis; (3) rarefying osteitis; and (4) spontaneous fracture of the exhausted bone. Such fractures (with their initial periostitis) have been noted in many bones, particularly in the tibia, fibula, femoral shaft and neck, the humerus, calcaneum, and so forth. Perthes' and Koehler's diseases may conceivably be examples of these overload injuries.

In hypertrophic pulmonary osteoarthropathy (Marie-Bamberger syndrome), there is a proliferation of the inner periosteal layer with calcification and an irregular layer of subperiosteal new-bone formation. Associated with chronic affections of the lungs and mediastinum, the syndrome results in clubbing of the fingers and toes, and less frequently in painful enlargement of the long bones of the forearms and legs. The osteodermopathic syndrome,[9] called "acropachyderma with pachyperiostitis" by Brugsch, represents a systemic overgrowth of bones and skin with leprous disfiguration of the face and extremities similar to those of the patients with pulmonary osteoarthropathy.

Neuhauser[10] has recently described a progressive diaphyseal dysplasia in children with thickening of the periosteum. In these cases the cortex has also been altered with progressive bone resorption as well as deposition. In leucemia,[11] there may appear a lamellated type of periosteal new-bone formation, but it is associated with cortical osteoporosis and marrow expansion; though interesting, these signs are not pathognomonic. Periosteal reactions have also been recorded in tuberculosis,[12] neuroblastoma, chloroma, and in chronic arsenic and phosphorus poisoning.

The foreign literature, largely unavailable to the practicing pediatrician, makes sporadic mention of periostitis: Snorrason writes on "Tibial Periostitis" in a Belgian journal, Grosz described a "Periostitis of the Tibia" in a Budapest publication, while in a French journal appears an article on "Diaphysary Osseous Rarefactions (Ossifying Periostitis)." In German is found "Hyperplastic Periostitis in Adolescents" and "Traumatic Periostitis Ossificans," as well as "Traumatic Periostitis of Femur Erroneously Diagnosed as Sarcoma. . . ."

In English, however, previous mention of this condition seems limited to

two articles by Snedecor and his associates[13, 14]; these refer to "Traumatic Ossifying Periostitis of the Newborn," a condition occurring as a direct sequel to breech delivery. Snedecor states that the essential lesions shown in the roentgenograms of his eleven patients follow a pattern of epiphyseal separation, periosteal stripping, or a combination of both, but in older children it is our observation that the periostitis is confined to the diaphysis, and does not extend into the epiphyseal zone. In no one of our cases of traumatic periostitis has injury occurred to the epiphyses. Smyth and his colleagues express skepticism that trauma is of etiological importance in the original cases described by Snedecor, and Smyth points out a similarity of roentgenographic findings between Snedecor's traumatic periosteal reactions and his own infantile cortical hyperostosis. Snedecor's more recent observations, plus our own case histories, would suggest that Smyth's doubts were unfounded.

CASE 1.—N. M., a 1-year-old girl, was standing against a chair when she accidentally fell, twisting her left leg beneath her. A "snap" was heard, and the child would then not stand or place weight on the left leg, though she would crawl. It was stated that the child had "sprained her ankle." At examination three days after injury, there was some tenderness over the left lower tibia, with a sense of fullness here. X-rays were negative for bone injury, the hip joints were normal, and no soft tissue swelling could be demonstrated. The child began to walk again with assistance by the tenth day and became symptom-free. On the eighteenth day after injury, the child used both legs equally, but a follow-up x-ray clearly showed a marked periostitis of the left tibia.

CASE 2.—R. S., a 2-year-old boy, had been treated for a "sprained left ankle" by an out-of-town physician. Though the initial x-ray was entirely normal, a plaster boot had been applied and kept in place for fourteen days. In removing the cast, however, the electric saw accidentally lacerated the dorsum of the foot, with an ensuing indolent lesion that healed slowly. Because of low-grade fever for a few days, plus failure of the foot to heal, our first x-ray film was taken seven weeks after injury; an advanced periostitis of the middle one-third of the left tibia was present, but the child had been walking normally ever since the removal of the cast.

CASE 3.—S. M., a 5-year-old girl, had been limping on the left leg for about two weeks. She had not been ill, and did not complain, nor was a definite history of injury obtained in this instance. Examination showed some tenderness along the medial surface of the left tibia, and x-ray revealed a periosteal reaction in the region of the junction of the middle and upper thirds of this bone. One week later the x-ray picture was unchanged, but the limp had virtually disappeared, and subsequent recovery was uneventful.

CASE 4.—B. S., a 5 pound, 15 ounce breech-born infant of a gravida ii mother, showed arthrogryposis multiplex congenita, with bilateral congenital dislocation of the hips; after discharge from the newborn nursery, the infant received daily physical therapy and passive exercise for joint stiffness.

X-rays on the third day of life showed normal bone structure, except for the hip joints. At 7 weeks of age, while the mother was exercising the right knee joint, a snapping sound was heard, following which the infant cried for several hours and subsequently whenever the right leg was touched. X-rays on the day of this injury showed a fairly early periosteal

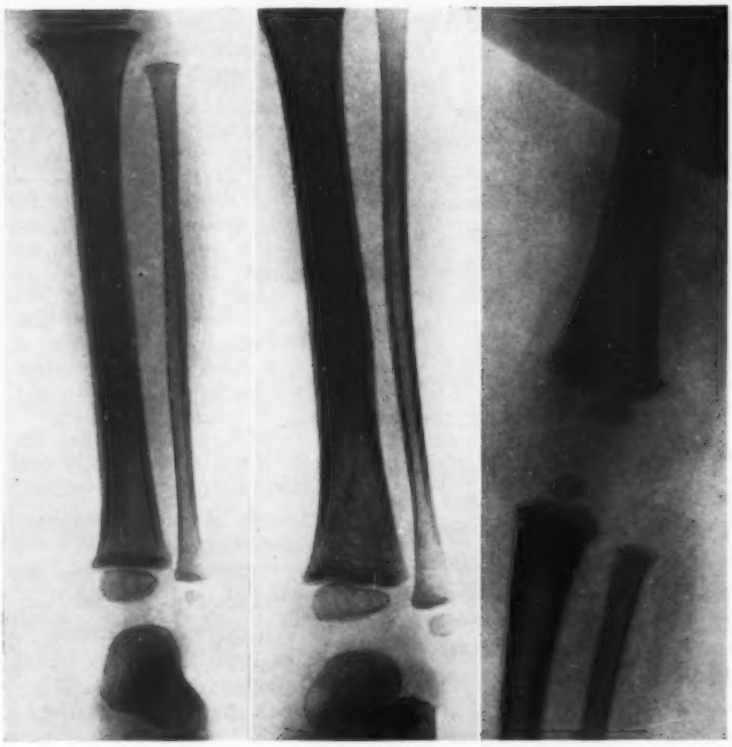

Fig. 1. Fig. 2. Fig. 3.

Fig. 1 (Case 1).—Traumatic periostitis of tibia, eighteen days after injury. X-rays on third day after injury entirely normal.
Fig. 2 (Case 2).—Advanced tibial periostitis seven weeks after "ankle sprain."
Fig. 3 (Case 4).—Periosteal reaction of femur, secondary to manipulative exercises.

reaction of the right femur posteriorly; this lesion was too recent to be associated with birth trauma, and too old to be related to the immediate injury, but must have been incurred during prior manipulation. A follow-up film was not obtained until the twenty-fourth week, at which time there was noted only a double contour of the right femur laterally.

CASE 5.—J. J., a 9-month-old infant, had twisted his right leg in falling in his crib. Thereafter he cried whenever his shoes were put on and when the right shank was touched. Three days after injury, we thought the pathology was that of a sprain, and suggested x-ray later if the child did not improve. An x-ray on the seventh day showed a very early fine line along the medial aspect of the right tibia.

CASE 6.—R. H., a 5-month-old male infant, had been in a foster home under supervision of the State Welfare Department until ten days before our initial examination. Because of apparent shortening of the right leg, an x-ray film of the hip joints was undertaken; both hip sockets were normal, with an acetabular index of 27 degrees bilaterally, but a double contour of the lateral femoral margins was apparent. This double contour could

Fig. 4 (Case 6).—The double cortical contour, a normal finding in infants.

readily be confused with a late resolving periostitis.

The more chronic type of limp is exemplified by:

CASE 7.—E. D., a 3-year-old girl, had been limping intermittently for about six months. One evening after watching a motion picture, the symptom apparently became intensified, so that the child refused to walk. Roentgenograms of the lower extremities revealed normal hip joints and long bones; the left ankle was also normal, but the right tarsal navicular bone showed flattening, fragmentation, and sclerosis—a characteristic picture of aseptic necrosis.[15]

By no means, however, do we mean to imply that all limps are due to periostitis. In general, those of short duration (a day or two) must still be classified as a sprain, while only a certain proportion of those of longer duration develop positive x-ray signs. Though we have no reliable figures to show the exact incidence of traumatic periostitis, the ability of two practicing pediatricians to collect five cases in less than a year serves to emphasize its relative frequency.

SUMMARY

The acute limping leg of early childhood, traumatic in origin, is frequently the result of periosteal separation. Roentgenograms delayed beyond the point of clinical recovery will demonstrate an ossifying periosteal reaction in many cases. Ultimate radiologic resolution is complete.

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MAJOR HEREDITARY ECTODERMAL DYSPLASIA

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HEREDITARY ectodermal defects are not uncommon. Alopecia, defects of the nails, and like disorders of hereditary origin occur frequently in some areas.[1] Such conditions are usually not physically incapacitating, but some of them do impose extraordinary problems upon the individual in the area of mental and social adjustment. The cases described here present a picture of ectodermal defect sufficiently severe to cause serious psychological problems and some degree of physical incapacity.

Cases of "major" hereditary ectodermal dysplasia are comparatively rare in the literature. However, the symptoms of the various cases which have been reported are so similar, that they may be considered to constitute a definite syndrome.

Briefly, the symptoms are these. The skin is dry, smooth, and pliable. There is a complete or nearly complete absence of sweat glands (except axial), sebaceous glands, and hair follicles. Lanugo hair is absent. Scalp hair is sparse, dry, and brittle. The forehead is usually prominent, and the nose malformed (saddle nose). The lips are thick and muscular. There may be no teeth or a few malformed ones. The nasal cavities are often malformed, and the senses of taste and smell may be impaired. Finally, a tendency toward mental deficiency has been noted.

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In consequence of the absence of sweat glands, heat regulation is defective. When resting under normal temperature conditions, insensible perspiration is normal and body temperature is normal. However, when the environmental temperature is high or the individual is engaging in strenuous physical activity, the body temperature rises rapidly.[2] During the summer months the individual is fatigued and apathetic, and often collapses if subjected to too much heat or exertion.

Of the symptoms listed, three seem to be of special diagnostic value: hypotrichosis, anhidrosis, and adontia. Many patients with hereditary ectodermal dysplasia have only one or two of these symptoms rather than the entire syndrome. The term *major hereditary ectodermal dysplasia* as used here will refer to the above triad of symptoms plus ancillary symptoms. This disorder seems to be sex-linked with males displaying the symptoms and females acting mainly as transmitters.[2, 3, 4] However, in one case reported, a female exhibited the full syndrome.[3] Some of the "lesser" forms of hereditary ectodermal dysplasia are transmitted in other ways (e.g., as simple Mendelian dominant characters[1]).

CASE REPORTS

The two patients (Paul and William) reported here are brothers. They are the eighth and tenth children in a family consisting of five

brothers and five sisters. Another male, the third child in order of birth, is also said to have the symptoms of major ectodermal dysplasia, but he was not available for examination. As far as is known, this is the first report of three cases in one sibling group, although several earlier cases came from large families. The eldest sister is reported to have a son who resembles William and is a "nonsweator." This child was not available for examination.

The six youngest of the ten siblings were admitted to Mooseheart on July 13, 1943. Both parents are dead. The peculiar appearance and defects of Paul and William were noted at time of admission, but were first ascribed to malnutrition and avitaminosis. William's blood test showed hemoglobin 55 per cent, but this condition quickly improved. Aside from this and the symptoms to be described, the boys were healthy.

At this writing Paul is 18 years, 1 month of age and William 13 years, 9 months of age. William is a classic case of major ectodermal dysplasia. In Paul some of the symptoms are less pronounced.

General Appearance.—The appearance of William (Fig. 1 *A* and *B*) is typical. His weight is 107 pounds, height 61 inches, and his musculature is well developed. The appearance of Paul (Fig. 1 *C* and *D*) is somewhat better. His nose, forehead, and lips present more normal contours, and the contour of the lower face has been much improved by dental correction. His weight is 170 pounds and height 72 inches.

*Hospital Reports.**—William's latest laboratory reports from the hospital show the following: red blood count 4,800,000; white blood count 7,500; hemoglobin 80.96 per cent; cholesterol 160 mg.; pulse 76; blood pressure 88/58; basal metabolic rate + 29; urinalysis negative. Paul's latest report shows the following: red blood count 5,200,000; white blood count 9,500; hemoglobin 86.12 per cent; cholesterol 130 mg.; pulse 56; blood pressure 100/71; basal metabolic rate + 3; urinalysis negative. Wassermanns given at time of entry (1943) were negative.

Skin.—William reports that he has never sweated except in the armpits and occasionally a little on the palms. His skin is smooth and dry with no trace of pores nor lanugo hair. Paul presents almost the same picture, but reports that he has occasionally sweated a little over small areas. Paul suffers from cronic eczema of the lower arms and hands.

Biopsies were performed in February, 1950, on both boys and upon their brother, who is a normal sweator. An elliptical piece of skin about 15x4 mm. in area and 4 mm. thick was removed from the left scapular area in each case. The pathologist's report indicated that in the specimen from Paul there were no hair follicles or sweat glands in the underlying corium, which appeared normal in all other respects. In the specimen from William there was one hair follicle with sweat gland in the corium. In the specimen from the normal brother there were two hair follicles with adjacent sweat glands and two groups of eccrine glands.

X-rays.—Skull X-rays showed the clinoid processes joined over the sella in both cases. X-ray of Paul revealed pronounced prognathism. X-rays of hands and long bones showed no abnormalities in either case.

Hearing and Speech.—An audiogram obtained on William in December, 1948, showed severe hearing loss: 90.5 per cent for the left ear, 98.3 per cent for the right ear, and 91.45 per cent for the combined ears. An audiogram obtained in May, 1950, by the same examiner showed the following losses: 8.0 per cent for the left ear, 11.7 per cent for the right ear, and 11.35 per cent for the combined ears.

*These reports and the x-ray and biopsy reports were obtained through the kind cooperation of Dr. E. S. Denney, Director of Health, Mooseheart, Dr. B. E. Moisant of Aurora, Ill., and Miss Dorothy Nelson, Supervisor of the Mooseheart Hospital.

Fig. 1.—*A*, William, aged 7 years. Note thin, unruly hair, sparse eyebrows, saddle nose, thick lips. *B*, William, aged 13 years, 7 months. Hair thicker and better controlled; other features still pronounced. *C*, Paul, aged 13 years. Note sparse eyebrows, lip contours. Features as a whole are better formed than William's. *D*, Paul, aged 17 years 11 months. Thinness of hair more apparent than in *C*. Note improvement in lip contours since dental correction; prognathism.

The difference is striking, especially in view of the examiner's opinion that good cooperation on the test was obtained on both occasions. The factors which may be responsible for so great an improvement are (1) the time of year—William suffers from head colds in the winter which apparently affect his hearing; (2) William had been suffering from chronic otitis media, which has cleared up in recent months; and (3) the wearing of an electronic hearing aid, which by making a wider variety of sounds available to him, may have enabled him to learn to respond to what he does hear. The otologist's report indicates a slight retraction and decreased reflexes of both tympanic membranes.

Paul's hearing loss is slight, but it does interfere sometimes with his ability to apprehend speech. He, like William, has in the past suffered from chronic otitis media.

William's speech is thick and slurred. There is a notable inefficiency in pronouncing sibilants, and his inflection is poor. These difficulties are attributed both to his inability to hear the speech of others clearly and to the extremely poor condition of his teeth. Paul's speech was slightly defective, but is now greatly improved due to dental correction and speech courses in high school.

Vision.—William's vision is 20/25 uncorrected, and he has a very slight strabismus. Paul's vision is 20/20 uncorrected.

Smell.—Careful tests have not been carried out in this area, but some deficiency does seem to be indicated. The odor of such strong-smelling substances as acetone, chloroform, ether, and a very spicy-smelling commercial mouthwash do not seem to be fully appreciated. The otologist's report (1949) states that William will probably continue to have nasopharyngitis because of the size and contour of the nasal vestibule, and that this will in turn affect his hearing. As previously indicated this condition seems to have improved spontaneously, at least temporarily.

*Dentition.**—As of February, 1944, at the age of 12 years, Paul's dental equipment consisted of ten permanent and four deciduous teeth; four of the former were malformed. Full mouth x-ray revealed an unerupted peg-shaped lower left cuspid; all other teeth were missing. By June, 1945, the lower left permanent cuspid had erupted into the mouth, but otherwise no changes had taken place (Fig. 2 *A*). Normal dentition for his age (13 years) would have been twenty-eight teeth erupted and four third molars unerupted.

When orthodontic treatment proved inadequate it was decided to resort to prosthetic dentistry. The lower missing teeth were replaced with bridgework and the upper teeth removed and replaced with a full upper denture (Fig. 2 *B*).

In July, 1948, at the age of 12 years, William possessed six erupted permanent teeth, six erupted deciduous teeth, and five unerupted permanent teeth (Fig. 2 *C*). Of these, seven were malformed. By January, 1950, the lower left deciduous second molar had been replaced by the lower left permanent bicuspid and a malformed upper right permanent cuspid had erupted distally to the deciduous cuspid, instead of replacing it (Fig. 2 *D*). Therapy similar to that executed on Paul will be undertaken on William in the near future.

Effects of Temperature Variation and Exercise.—Both boys suffer greatly during the hot periods of summer. They become slow and apathetic, and sometimes dizzy or faint. These symptoms are much more pronounced in the younger boy, William, who occasionally collapses. Strenuous exercise produces similar results in William, especially dizziness. Paul manages to engage in some sports, but can

*We are indebted to Dr. J. M. Williams of the Mooseheart Dental Department and Aurora, Ill., for the data in this section and for permission to publish the photographs of the dental casts (Fig. 2).

exert himself more during cool weather. Both boys are most comfortable during cool seasons, but they report suffering from cold during the winter.

Experimental Tests.—In December, 1949, both boys were subjected to two experimental physiological stress conditions, a 90-second period of hyperventilation and the cold pressor test. During these tests the following were recorded continuously: electrocardiogram, electroencepalogram, electromyogram (frontalis muscle), palmar skin potentials, and respiration. All of the tracings, except respiration, were recorded by means of an Offner electroencephalograph, Model A, with Crystograph recorder.

Both scalp-scalp and scalp-ear lobe electroencephalograms were recorded from the frontal, sensory-motor, and occipital regions bilaterally. William's record showed normal brain electrical rhythms with a slight tendency toward amplitude asymmetry. His occipital alpha frequency was 11.1 per second, the upper end of the normal frequency range for his age group. Paul's record was at best questionably normal. All activity was of relatively low voltage, and the occipital alpha rhythm was rarely seen. The most persistent activity consisted of low-voltage 4 per second waves. Neither boy showed the development of high-voltage 3 per second waves during hyperventilation, although both became very dizzy. William became so dizzy in fact that he stopped deep breathing after just 50 seconds, and still showed signs of dizziness 30 minutes later upon arising from the experimental couch. Most children of his age have little difficulty in maintaining deep breathing for 90 seconds.

During his brief period of hyperventilation, William's heart rate increased to a maximum of 35 beats per minute above his normal resting heart

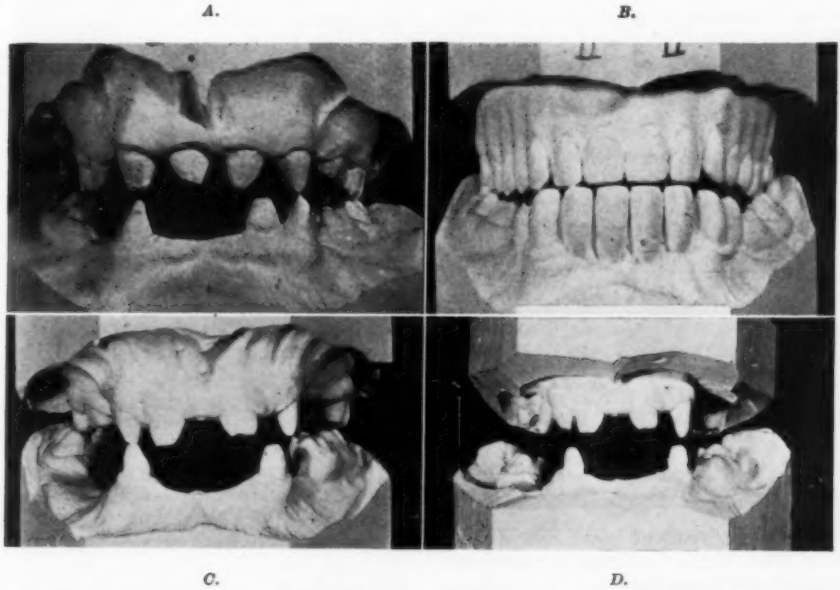

Fig. 2.—Shows dental condition typical in hereditary ectodermal dysplasia. Casts have been placed in end-to-end bite for photographic purposes. *A*, Cast of Paul's teeth following unsuccessful orthodontic treatment (1945). *B*, Cast of Paul's teeth following prosthetic dentistry as described in text (1947). Of the teeth visible only the lower molars are natural. *C*, Cast of William's teeth (1948). *D*, Cast of William's teeth (1950) showing changes described in text.

rate, and after he stopped deep breathing showed pronounced fluctuation for 3 minutes before it returned to normal. The average maximum heart rate increase for ten normal controls was 19.3 beats per minute with a range of 9 to 28 beats per minute. Paul's maximum heart rate increase during 90 seconds of deep breathing was 42 beats per minute with recovery to normal in 50 seconds.

The cold pressor test was administered according to the method of Hines and Brown,[5] mercury sphygmomanometer readings being taken at the standard intervals along with the other measures previously mentioned. William's maximim blood pressure increase during the test was 11 mm. Hg systolic and 10 mm. Hg diastolic with recovery within 2 minutes. The electrocardiogram showed pronounced heart rate fluctuation which lasted for over 3 minutes after the end of stimulation. This fluctuation was noted again on a repeat test. William's electrocardiogram is also characterized by a very pronounced sinus arrhythmia.

Paul's maximum blood pressure increase during the test was 22 mm. Hg systolic and 16 mm. Hg diastolic with recovery taking 5 minutes, a hypertensive response. His heart rate, too, showed irregular fluctuation, particularly after the end of stimulation. This is in contrast to ten normal controls who showed rather smooth small to moderate rises in heart rate during cold stimulation, followed by uneventful returns to normal.

Galvanic skin responses (GSRs) could be recorded from these boys, but they were generally weaker than those of normal children and a large number of them were of abnormal waveform. These facts are pertinent to the question of whether the GSR is basically a secretory or a vasomotor phenomenon,[6] but unfortunately they do not provide a clear-cut test, because (1) the boys do sweat to some extent on the palms, and (2) the boys suffer from a number of other deficiencies—including some vasomotor disturbance as has been shown—so that sweat gland deficiency is only one of a number of variables. However there did seem to be a correlation between moistness of the palms and the size and "normality" of the GSRs obtained.

Psychological Status.—Intellectually, William is dull (I.Q. 78). From 1943 to the present his educational age has lagged behind his chronological age by an increasing amount. The difference is now over two and one-half years. His school grades have been mediocre to poor.

Intellectually, Paul has fared somewhat better. His latest I.Q. was 94. His educational age has remained constantly about one and one-half years behind his chronological age. His grades are fair to average.

Insofar as social adjustment is concerned, William has been since his arrival, and still is, a behavior problem. He feels that he is generally rejected by other people. He tends to take advantage of his physical disability and malingers when he can "get away with it." Although he is in good contact with present reality, he seems unable to plan for the future in realistic terms. He aspires to roles which are far beyond his capacities—veterinarian, doctor, engineer—and his plans vary a great deal from day to day. In short, abstract reasoning, value judgments, and concepts of the future are difficult for him to handle.

Rorschach findings in general substantiate the clinical impression. In addition to the low average intellectual ability, there is a defective emotional and social development. He is incapable of relating to human figures except on a purely superficial level and gives no indication of any mature emotional reactions. There are few external resources open to him for his interests are narrow to the point of rigidity and infantile in nature. Most of his responses are of the easy conventional type; even when he follows his tendency to select the unusual, he attempts to maintain intellectual con-

trol by assigning them simple interpretations. For the most part he seems unable to respond to or handle emotional situations, but occasionally an infantile, unpredictable outburst will occur. Recovery from such incidents is immediate, complete, and accompanied by an apparent lack of insight. A basic pattern of hostility and aggression occasionally gives rise to anxiety but this too is of a superficial and fleeting nature.*

It is believed that his psychological maladjustment is to some extent a secondary complication of his primary disorder, which obviously makes social intercourse difficult. Since relief from the primary disorder is impossible, psychotherapy has been employed in an attempt to improve his adjustment. The results have thus far not been encouraging.

Paul does not present as severe an adjustment problem as William. However, he is not ideally adjusted. He tends to be self-effacing and show other signs of inferiority feelings. Probably because of his modest nature he is better liked than William. It is felt that if Paul can be directed into a vocation which will be interesting to him and commensurate with his abilities and especially his physical limitations, he will make an adequate adjustment after he is graduated from Mooseheart.

DISCUSSION

So many forms of hereditary ectodermal dysplasia and so many miscellaneous symptoms have been reported that it is extremely difficult to tell whether any given symptom is directly connected with the ectodermal dysplasia or is merely coincidental. However, a number of features of the cases reported here and of earlier cases, together with embryological data, combine to suggest that the nervous system and related structures as well as the skin may be involved in many cases of ectodermal dysplasia. Such features are deviant autonomic (blood pressure and heart rate) responses to mild physiological stress, a questionable electroencephalogram, borderline mentality, and symptoms of endocrine dysfunction. A large majority of reported hereditary ectodermal dysplasics are below normal in intelligence,[4] and a number of cases of "subtotal" ectodermal dysplasia with extensive and severe neural defects have been reported. The peripheral defects are, of course, of major importance in the present cases, but the signs of neural and endocrine involvement seem definite. The degree of involvement of the nervous system in ectodermal dysplasia probably depends upon how early in the embryonic period the dysplasia becomes manifest —the earlier, the more severe the involvement.

In any event, careful and extensive study of each individual case of hereditary ectodermal dysplasia is indicated, since many various defects usually accompany the primary symptoms. It is possible that this disorder, as well as "subtotal" manifestations of the syndrome, is more common than the sparcity of reports in the literature implies. It may be that many such cases have been misdiagnosed as avitaminosis, congenital syphilis, etc.

Finally, it is worth while pointing out that, as in all cases of visible disfigurement, the physician should be aware of the possibility of psychological maladjustment and recommend psychotherapy in those cases in which it seems warranted.

The writer is indebted to Dr. Martin L. Reymert, Director of the Mooseheart Labora-

*Rorschach's test was administered and interpreted by Miss Jean Waldvogel.

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SITUS INVERSUS

Report of Three Cases and a Review of the Literature

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THE anomaly of complete reversal of all organs of the body is not a common one. The incidence of this abnormality is difficult to determine since the condition is compatible with apparently normal life, and exists in many individuals undiagnosed. The purpose of this report is to present three such cases which were complicated by other conditions, and to review briefly the available literature.

LeWald[1] (1925) reported twenty-nine cases in 40,000 roentgen-ray examinations of the chest and digestive tract, with an incidence of approximately one case in 1,400. Sherk[2] (1922) of the Mayo Clinic observed complete transposition of the viscera ten times in 347,000 admissions. Adams and Churchill[3] state that situs inversus occurred twenty-three times in 237,112 admissions to Massachusetts General Hospital. Vineberg[4] reviewed the literature in 1946 and found 475 cases reported to that date. He quotes Larson who, in 1938, reported an incidence of one case in 10,000. Parson[5] (1945) reported two cases of complete situs inversus in approximately 15,000 private patients. Physical examinations of United States Army recruits (1947) revealed an incidence of one case in 35,000. These findings were confirmed by appropriate gastrointestinal studies.[6, 7] Situs inversus has been discovered three times in 51,246 admissions to George Hubbard Hospital.

From the Department of Pediatrics, George Hubbard Hospital of Meharry Medical College.

Table I. Frequency of Situs Inversus According to Various Authors

Author	Year	Frequency
Sherk	1922	1:34,700
LeWald	1925	1:1,400
Adams & Churchill	1937	1:10,300
Parson	1945	1:7,500
U. S. Army Recruits	1947	1:35,000
Tanner-Cain & Crump	1950	1:17,000

Many theories, seeking to explain the etiology of this condition, are to be found in the literature. Virchow discovered that in situs inversus the umbilical cord was wound spirally to the right, whereas the reverse is normal. He felt that this was a determining factor. An embryological change in the "S" shape of the cardiac tube, with the right side placed nearest the blood supply in the embryo, has also been considered a cause.[2] An additional hypothesis suggests that the condition is related to the survival of one of a set of twins, in which case the establishment of symmetry and asymmetry in the blastoderm preceded the twinning.[4-8] More recent studies[8] of the problem of asymmetry in the viscera suggest that the prime determining factor is the normal spiral organization of the developing gut, which when reversed in direction automatically leads to transposition. Vineberg[4] points out that Cockayne (1938)

studied family pedigrees and found that situs inversus was a recessive character caused by a single autosomal gene.

CASE REPORTS

CASE 1.—J. N., a newborn Negro female, was delivered on the obstetrical service of George Hubbard Hospital April 15, 1939. The infant weighed 3.49 kilograms (7 pounds, 11 ounces) at birth. The crown-heel length was 51 cm. Respirations were good, and no resuscitation was given. Labor was five hours and delivery normal.

The mother was a 24-year-old unmarried gravida i, para i, who had had an uneventful full-term pregnancy. Her serological test for syphilis was negative during pregnancy. The family history was noncontributory.

On April 16, the infant suddenly developed cyanosis and vomited dark bloody material. Physical examination revealed dyspnea, cyanosis, stupor, harsh breath sounds, and râles in both lung fields. The temperature was 37° C. (98.6° F.) and respirations 46 per minute.

A portable x-ray chest plate showed a shift of the mediastinal contents toward the right side, with a slight increase in the width of the upper mediastinal shadow. The gas-filled stomach was noted to be on the right side, suggesting situs inversus. The leaves of the diaphragm were equal in height. The size and shape of the heart as well as its disposition in the chest were not compatible with dextrocardia, nor was any other congenital cardiac anomaly suggested during this examination.

Serological test for syphilis was negative.

The infant was placed in an incubator, given continuous oxygen, and alpha-lobeline as needed. Cyanosis persisted from birth with only slight improvement during oxygen administration; the course was progressively downhill, and she expired on April 18, 1939. Clinical diagnoses included congenital heart disease, situs inversus, and enlarged thymus.

Post-Mortem Examination.—

Gross: The right lung was observed on the left side and the left lung on the right. The heart was normally placed, was extremely dilated, and showed many gray areas of patchy distribution, both on the surface of the left ventricle posteriorly and on the surface of the right ventricle anteriorly. There was immense thickening of the myocardium and endocardium. The latter was covered by a fine granular substance simulating an organizing thrombus. Small areas of questionable infarction were observed. The mediastinal space showed a reversal of the thymus, in that the greater portion of the organ formed a constricting collar around the vessels of the upper anterior mediastinum.

Peritoneal cavity: All of the abdominal organs were reversed.

The kidneys showed polycystic changes bilaterally.

All of the organs were preserved in situ, and hence not weighed.

Microscopic: Sections from the heart revealed infantile muscle fibers in which congestion and edema were the most outstanding changes.

The lung showed congestion, edema, hemorrhage, and in places was emphysematous.

The kidney sections showed polycystic changes.

Pathological diagnosis: Situs inversus, compression of the aorta by a displaced thymus, organizing endocarditis, infarction of the heart and lung, urethral atresia, bilateral polycystic kidneys.

CASE 2.—J. F., a 10-month-old Negro female, was admitted to the pediatric service of George Hubbard Hospital (Dec. 29, 1947) with a chief complaint of a "cold" and vomiting of three weeks' duration. The mother was unable to give a satisfactory history of the present illness.

The baby was born at home (Feb. 2, 1946), weighing 2.73 kilograms (6 pounds), after a period of gestation estimated to be nine months.

The mother, aged 33 years, was a gravida viii, para vi, and showed obvious mental deficiency. She had aborted twins once after four months of gestation. Her blood serological reaction during the pregnancy involving the patient was reported as negative, and she gave no history of any previous antisyphilitic therapy. The father died March 28, 1947, at the age of 74 years. He had been inadequately treated for syphilis and was known to have had syphilitic aortitis. The five living siblings were said to be well although one child had had convulsive seizures during infancy. One male child died at the age of 4 weeks with bronchopneumonia.

The patient had been artificially fed since birth on an evaporated milk formula and had been given cod liver oil and orange juice at irregular intervals. She had received no solid food and was said to have customarily passed one hard stool daily. Routine immunizations had not been completed.

The past history was significant in that the infant had had two previous hospitalizations at 6 and 8 months of age for severe respiratory infections. Her hospital record revealed that the following diagnoses had been made on these previous admissions: bronchopneumonia with empyema, dextrocardia with situs inversus (Fig. 1), congenital heart disease (Fig. 2), type undetermined, and mongolism.

Physical examination, at the time of the present admission, revealed a moderately dehydrated, malnourished female infant in acute respiratory distress. Admission weight was 6.25 kilograms (13 pounds 12 ounces), crown-heel length 60 cm., head circumference 44 cm., chest circumference 39.5 cm., abdominal circumference 42.5 cm., temperature 39.7° C. (103.6° F.), pulse 196 per minute, and respiratory rate 96 per minute. The pharynx was acutely injected, a mucopurulent nasal discharge was present, and the tympanic membranes were slightly inflamed with normal light reflexes. The facies had mongoloid characteristics. The point of maximal impulse was noted to be in the fourth right intercostal space, and percussion dullness could be elicited for more than 3 cm. lateral to the right sternal border. No thrill was present. A loud harsh systolic murmur was best heard at the apex. Moist râles could be appreciated over both lung fields, but there was no evidence of consolidation. An abdominal mass was palpated 3 cm. below the left costal border, and an umbilical hernia was present. There was generalized muscular hypotonia and hypermobility of all joints. The hands were observed to be spadelike, with shortening and incurving of the fifth fingers. All reflexes were normal.

Fig. 1.—Case 2, J. F., aged 7 months. X-ray and barium study showing dextrocardia, right-sided stomach, and left position of the liver.

The hemogram on admission showed red blood count 4.61 million per cubic millimeter, hemoglobin 12 Gm., white blood count 14,900 per cubic millimeter with polymorphonulears 72 per cent, lymphocytes 28 per cent. Nose and

throat cultures yielded pneumococci. Blood culture was negative. Erythrocyte sedimentation rate was 3 mm. in one hour (Westergren). Blood chemistry on admission: nonprotein nitrogen 21 mg. per cent, serum cholesterol 85 mg. per cent, and chlorides (as sodium chloride) 492 mg. per cent. The Schick and the Mantoux tests were negative.

Admission x-ray examination of the chest revealed thickening of both hilar regions with exaggerated peribronchial markings.

She could not hold up her head nor could she sit. The grasp reflex was quite prominent. Compared with normal developmental standards, her level suggested that of a 3-month-old infant.

The patient was discharged on Jan. 20, 1948, but the mother failed to come for the baby when notified. Sulfadiazine was administered during this extended period of hospitalization, and the patient remained temporarily symptom free, except for persistent constipation which was intermittently relieved by enemas.

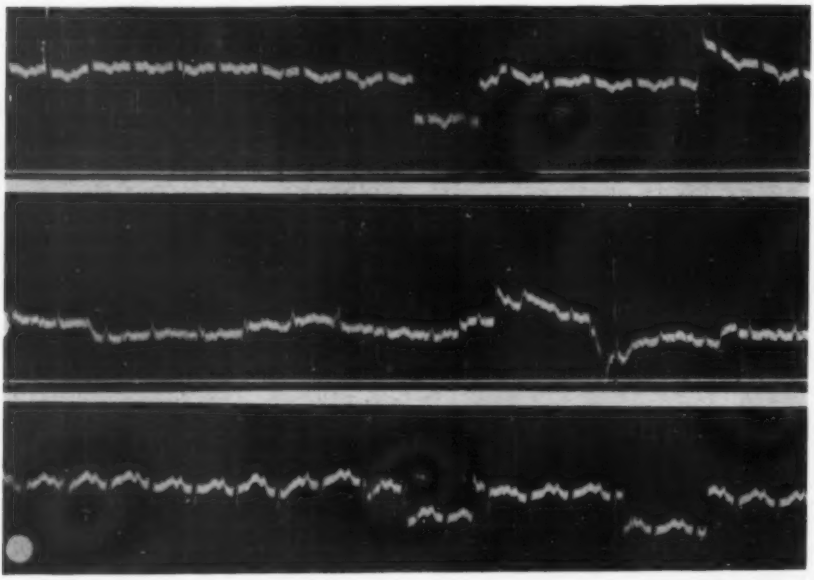

Fig. 2.—Case 2, J. F., aged 9 months. Electrocardiogram tracing showing sinus tachycardia. A-V rate 166 per minute. P-R interval 0.12 sec., QRS complex 0.04 sec. The tracing was compatible with dextrocardia.

The infant was given oxygen, penicillin 10,000 units every three hours intramuscularly, and fluids subcutaneously. Shrinkage of the nasal mucosa was attempted, and vitamin supplements were administered.

On this regime, the infant's response was considered satisfactory, and after a two-week period the temperature was stabilized within normal limits. During this interval, the patient's developmental status was roughly evaluated.

On January 26, the infant's temperature suddenly rose to 40° C. (104° F.). She did not appear acutely ill, and physical findings were not helpful. The hemogram and sedimentation rate were within normal limits. Subcutaneous fluids and tap water enemas provided only temporary remissions from hyperpyrexia. An x-ray picture of the chest showed clearing of the hilar thickenings and peribronchial markings. On January 31, the infant developed acute bilateral otitis media.

Penicillin therapy was reinstituted, 10,000 units every three hours intramuscularly. Sulfadiazine was discontinued. The patient's temperature dropped to 37.6° C. (100° F.) within twenty-four hours.

On the morning of February 5, the temperature rose suddenly to 39.4° C. (103° F.), and the infant appeared dyspneic, with marked intercostal and subcostal retraction. Physical examination revealed only a hyperemic pharynx and a thick mucoid discharge in the oral cavity. No cyanosis was apparent. Hemogram showed red blood count 5.2 million per cubic millimeter, hemoglobin 9 Gm., white blood count 13,000 per cubic millimeter with a normal differential. Urinalysis was normal with the exception of 6 white blood cells per high power field.

The patient was placed in an oxygen tent and given parenteral fluids subcutaneously and intravenously. Penicillin was increased to 20,000 units intramuscularly every three hours.

Six hours later, the temperature rose to 42.1° C. (108° F.) rectally, and she was observed to have repeated tonic convulsive seizures accompanied by grunting sounds. The dyspnea appeared more marked and the pulse rate was 120 beats per minute. Rhonchi and harsh breath sounds were present throughout the chest.

A spinal tap done immediately revealed crystal clear fluid, under no increased pressure, with normal chemical and cytological findings.

The infant was sedated with phenobarbital sodium, given alcohol sponges, tap water enemas, and continuous oxygen.

Despite the above measures, intermittent tonic convulsions continued. Twelve hours later, the temperature rose again to 42.1° C. (108° F.), and the patient expired (Feb. 6, 1948).

Post-Mortem Examination.—

Gross: Complete rotation of the thoracic organs was observed. The left lung was on the right side and the right lung on the left side. The apex of the heart was at the fourth right intercostal space.

The heart weighed 25 grams, had a widely patent foramen ovale, and no interventricular septal defect.

The lungs showed dark reddish discoloration peppered with petachiae. The peribronchial lymph nodes were enlarged, pale pink, and moderately soft. The main bronchus revealed a considerable amount of glairy mucus which almost occluded the lumen. The cut surfaces of the upper portion of both lungs were uniformly dark reddish brown and yielded a scant amount of blood in which no gas bubbles were visible. The lower portions revealed pink frothy material.

Peritoneal cavity: All organs were displaced. The liver was rotated to the left side, and the gall bladder appeared at a point slightly outside the left midclavicular line. The appendix was on the left. The stomach was rotated with the liver so that the pylorus was at the midline beneath the right lobe of the liver. A Meckel's diverticulum was observed in the primary portion of the lower part of the ileum. The pancreas was also transposed.

The kidneys were of average size, appeared bright reddish brown in color, and showed fetal lobulations. The cut surfaces revealed dilated calyces. The ureters were patent into the urinary bladder.

Gross observation and sectioning of the brain before and after formalin fixation revealed normal findings.

Microscopic: (Only the lung sections are reported, since other sections were not revealing.)

Sections from the lungs showed areas of congenital atelectasis, small areas of emphysema, and large areas of recent hemorrhage and edema. The large bronchioles were almost completely filled with muco-epithelial plugs. Cellular infiltration of the alveolar walls indicated interstitial reaction. A section from the trachea revealed moderately edematous intact mucosa in which there was a slight hyperemia. The submucosa was infiltrated with lymphocytes and occasional polymorphonuclear cells, and

the mucous glands were hyperactive and showed plugged lumens.

Pathological diagnoses: Chronic tracheobronchitis, atelectasis of the upper portions of both lungs, widely patent foramen ovale, situs inversus, Meckel's diverticulum, slight rickets, bilateral hydronephrosis and hydroureters (nonobstructive), hemosiderosis of the spleen, fatty metamorphosis of the liver.

CASE 3.—W. J. S., an 11-day-old Negro female infant, was admitted to the pediatric service of George Hubbard Hospital Nov. 11, 1949, with a chief complaint of shortness of breath.

The infant was the product of a full-term pregnancy, an eleven-hour labor, and a spontaneous delivery on Oct. 27, 1949, at a local hospital. She was discharged from the newborn nursery at 5 days of age, and the father noted that she immediately appeared short of breath and had rapid respirations. This condition became progressively worse daily. There was no history of cyanosis.

The mother, a 16-year-old gravida i, para i, was living and well, and the father, 21 years of age, was in good health.

Physical examination on admission revealed a pink well-nourished female infant in moderate respiratory distress. Temperature was 37.2° C. (99° F.), weight 3.2 kilograms (7 pounds), crown-heel 50.5 cm., head circumference 33 cm., chest circumference 31 cm., abdominal circumference 30.5 cm., respirations 76 per minute, and pulse 127 beats per minute. Positive physical findings included subcostal retractions with simultaneous head nodding. Percussion revealed increased cardiac dullness to the right and a harsh systolic murmur was heard over the entire anterior chest wall, with its maximal intensity to the right of the base of the sternum. A thrill of low intensity was appreciated on the right over the area of cardiac dullness, while an abdominal mass was palpated just under the left costal margin; no liver edge could be demonstrated on the right side.

Laboratory work on admission revealed blood count 3.23 million per cubic millimeter, hemoglobin 15.8 Gm., white blood count 13,000 per cubic millimeter, polymorphonuclears 52 per cent, lymphocytes 48 per cent. Urinalysis was normal.

X-ray of the chest November 8 showed a greatly enlarged cardiac shadow which almost completely obscured the right lung field. The left lung field and the right costo-phrenic angle were clear.

Barium swallows outlined a normal esophagus. The stomach occupied the right upper quadrant while the liver shadow was found to the left. A barium enema revealed the hepatic flexure on the left side and the splenic flexure on the right side high under the stomach.

An electrocardiogram taken November 8 showed right axis deviation. The auricular rate was 154, ventricular rate 154, P-R interval 0.12 sec., QRS complex 0.07 sec., and P_1 was inverted. The tracing was compatible with dextrocardia, and was repeated November 9 with the same findings.

The infant remained in the hospital from November 7 to 14, during which time she was maintained in oxygen continuously except when diagnostic or therapeutic procedures necessitated her removal for short periods of time. Fleeting attacks of cyanosis were observed upon withdrawal from oxygen. Although the patient remained afebrile and took an evaporated milk formula well, with no vomiting or regurgitation, her weight curve decreased steadily during hospitalization from 3.2 kilograms (7 pounds) to 2.75 kilograms (6 pounds, 1½ ounces).

At 1:50 P.M. on November 14, she vomited unobserved. When discovered, curds were seen passing from the mouth and nose. No respirations or heart tones were appreciated, and all measures failed to resuscitate the infant. The clinical diagnoses were: asphyxia due to aspiration of milk, congenital heart disease with intermittent cyanosis, dextrocardia with mal-

position of the great vessels, ventricular septal defect, and situs inversus.

Post-Mortem Examination.—

Gross: There was complete rotation of the heart and lungs. The heart was enlarged in all dimensions. The inferior and superior venae cavae opened into the right atrium, and the enlarged pulmonary artery was normally located despite the reversed position of the heart. Two of the pulmonary veins opened into the left atrium and two into the right atrium. The opened heart showed an extremely dilated right atrium which was almost continuous with the left, only a flap being present in the superior region of the normal septal location. The membranous portion of the intraventricular septum was absent. Coronary artery openings were normal.

The lungs were normal except for considerable atelectasis of the left lung.

The peritoneal cavity contained 15 c.c. of amber-colored fluid. All abdominal organs were in the reverse of normal position. The liver was larger than normal.

Microscopic: Heart sections were normal. The lungs showed marked fetal atelectasis, although the bronchioles appeared normal. There were small areas of emphysema with an accumulation of pigment-bearing (heart failure) cells.

The liver showed central glycolysis of the lobules with normal peripheral areas.

The thymus was poorly differentiated, and lymphoid elements occupied the bulk of the sections.

Thyroid sections showed no colloid present except for an occasional small abortive cystic dilatation containing semifluid colloid.

Pathological diagnoses: Anoxia, interauricular and interventricular septal defects, bilateral atelectasis, right-sided hypertrophy and dilatation of the heart, and situs inversus.

DISCUSSION

Situs inversus per se, in the absence of additional complicating anomalies, may remain undiscovered, and on occasion the presence of this condition can unexpectedly explain a left-sided attack of appendicitis. Many of the Army recruits (1947), in whom the condition was found, had no foreknowledge its presence. When discovered, therefore, it should be called to the attention of the patient or his parents so that this information may be made readily available to the physician attending the patient during acute abdominal episodes.

The three female infants included in this report all died within the first year of life, a fact which immediately suggests that other anomalies of a severe nature were present. Dextrocardia is ordinarily classified as an acyanotic congenital cardiac anomaly, and uncomplicated situs inversus is not known to cause death. Case 1 lived only three days and had persistent cyanosis, even in the presence of an oxygen atmosphere. The heart was in a normal position, although there was situs inversus of the abdominal viscera, and the lungs were found rotated. It is possible, therefore, to classify the case as situs inversus with a levocardia, and, as pointed out by Taussig,[18] this usually means that the heart has been rotated back to the left. Reference is made to three such cases that she has seen in which there was persistent cyanosis, and she states that a levocardia in a situs inversus is usually associated with extremely complicated cardia malformations. Case 1 is an exception in this regard, for it presented no anatomical defect of the heart. Early cyanosis in this patient may have resulted from compression of the aorta by a displaced thymus; later, infarction of the heart and lungs, and pulmonary edema undoubtedly served

as contributing factors. Case 3 revealed cardiac anomalies which alone were sufficiently extensive to account for cyanosis. Case 2, on the other hand, never appeared cyanotic.

Of the three cases, Patient 3 presented the most severe cardiac malformation. Two of the pulmonary veins opened into an extremely dilated right atrium which was almost continuous with the left, only a flap being present in the superior region of the normal septal location. In addition, the membranous portion of the interventricular septum was absent.

Extracardiac anomalies were restricted principally to the urinary tract in Cases 1 and 2. In addition, Case 2 revealed a Meckel's diverticulum, while Case 3 presented no significant malformations beyond those found in the heart.

The diagnosis of situs inversus was readily made clinically in both Cases 2 and 3, presumably because dextrocardia was presented in both. In Case 1, the gas-filled stomach on the right side, as observed on the x-ray film, suggested situs inversus. The location of the liver edge along the left costal margin is also a useful clue to the condition, and more especially so when the heart is found in the normal position. Once suspicion is aroused clinically, however, the diagnosis of situs inversus becomes somewhat routine in the application of electrocardiography and roentgenography, with contrast substances placed in the alimentary canal.

Fluoroscopy is more reliable than x-ray in the diagnosis of complete situs inversus, for as Taussig[18] points out, the condition may be such a perfect mirror image of the normal that unless careful regard is paid to the markings on the x-ray film, it is easy to reverse the film and read it as "heart normal in size and position." This relatively uncommon error was made on one of our cases.

Taussig[18] suggests that when dextrocardia is associated with an additional cardiac malformation, the clinical diagnosis may be extremely complicated. Such cases occurring in conjunction with situs inversus have been reported frequently enough to emphasize the clinical astuteness which the solution of these problems demand.[13-17]

It is interesting to note that the frequency of bronchiectasis and situs inversus occurring concomitantly has been reported to be significantly high.[3,4,7,9-12] Case 2 of this series, however, presented no clinical or pathological evidence of bronchiectasis, despite an unusual predisposition to severe recurrent attacks of tracheobronchitis.

SUMMARY

Situs inversus per se is a relatively rare and harmless condition, the incidence of which is unknown. This congential malformation was discovered three times in 51,246 admissions to Hubbard Hospital (1:17,000). Its clinical significance arises in the fact that it suggests the presence of other congenital malformations which may be seriously handicapping, and because it can on occasion explain otherwise bizarre findings during acute abdominal episodes.

Three cases are presented in female infants, all of whom died during the first year of life. Of these, one patient was found to have levocardia.

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CURRENT ADOPTION PRACTICES

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KNOWLEDGE concerning adoption practices is considered of importance to the pediatrician because in many instances he is called upon to care for the adopted child; at other times his advice is requested by parents on how to go about adopting a baby; many agencies call upon the pediatrician to assess an infant's physical condition and development prior to adoption placement. Adoptions have also a specific psychological aspect. Most agencies require a psychological examination of an infant or child prior to adoption. But more than that, adoption affects intimately the child's entire emotional, mental, social, and personality development. The adopted child also can profoundly change the behavior and development of the adopting family. Not without psychological import are the adjustments and emotional reactions of the natural mother in releasing her child for adoption; this latter problem is of course seen more frequently by the obstetrician and the social agencies.

In an attempt to bring more information to the professional public concerning these problems, a study was inaugurated by one of us (C. S. A.) to evaluate the adoption practices in the State of Connecticut. Although this study is confined to the practices of one state, most of the problems are countrywide with few exceptions. The Yale Clinic of Child Development had over a period of many years assisted the local adoption agencies in studying the child who is an adoption candidate. Before a new Connecticut law was passed, the only kind of adoption placement seen by the clinic was the planned, supervised, and protected adoption of the social agencies. But there is another kind which we have called the independent adoption where the placement is made directly by the natural mother or arranged by a relative, friend, doctor, lawyer, minister, and sometimes by a casual acquaintance.

Before the new Connecticut law, it was a rare family adopting independently who asked for any measure of the normality and fitness of the child they were taking as their own. But the new law requires a social agency investigation of independent adoption placements (after the placement has been made), a physical and mental examination of the child, and a probationary period of one year before legalization of the adoption. The law also provides for exceptions to these requirements. In the course of these investigations, the clinic was called upon to assist in the evaluation of the child. At first the idea of indiscriminate placement of children in adoption seemed primitive. As, however, most babies are pretty normal and most people pretty decent, it became apparent that many of these placements seemed per-

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fectly good. And then an extremely bad placement would turn up and point out that adoption is a serious matter, profoundly affecting the lives of at least three people, and that it does not seem right that it be entrusted to the law of averages. To test this point of view a series of both agency and independent adoptions was reviewed.

INDEPENDENT VERSUS AGENCY ADOPTIONS

In judging the infants and children, the results of our own developmental examinations are used. In judging the homes, we have the results of a social worker's investigation. Undoubtedly, some poor placements perhaps did better than anticipated; on the other hand, some good placements did not do as well as predicted. The study involves judgments made at the time of placement and does not include a long-range follow-up.

Of 100 babies placed independently, seventy-five were judged reasonably good babies who could be placed with reasonable safety into selected homes. That meant, of course, that twenty-five, or one out of four, were considered poor adoption risks, for one reason or another, such as mental retardation of varying degrees or serious personality defects. And it meant that twenty-five families assumed poor risks. Of the 100 families who adopted these babies, seventy-five were considered adequate, offering a reasonable modicum of security and stability, a happy home life and a decent up-bringing for the child. Our criteria were modest; we did not ask for perfection. Nevertheless, twenty-five families did not meet these modest standards for many reasons, such as an unstable marriage or an already broken home, undesirable mental health factors in either adopting parent, etc. In a few instances, there were histories of such items as alcoholism, prison records, prostitution, wife beating, and drug addiction in the adopting family's record. These are but the overt criteria which led us to call a home unsuitable; it can of course be assumed that there are many undesirable covert factors which are not listed in an ordinary investigation and which would adversely affect a child's development.

To return to the more favorable figures, the situation would not be as alarming if the seventy-five good babies were in the seventy-five good homes. The fact is that some of the good babies were in the unsuitable homes and some of the good families had poor babies. In only forty-six instances was the good baby and the good family together. In twenty-six of the fifty-four remaining cases the situation was questionable at best where a baby was seriously "overplaced" (a child of low but normal mental ability placed in a home where the cultural standards are high and expectations higher than the child can possibly meet and where a rejected and emotionally disturbed child can be anticipated) or where the natural mother is a potential troublemaker (she knows where the child is, visits, interferes, etc.). In the remaining twenty-eight cases, the family and the baby together produced a situation so undesirable that we felt the adoption should not be allowed and so advised the court. As court proceedings are confidential in such cases and not open to inspection, the ultimate disposition is not known.

In comparison, what about the babies placed under the supervision and guidance of social agencies, where an hon-

est effort was made to screen out the poor risks and the homes that were unsuitable? Of 100 agency placements seventy-six were good, i.e., seventy-six good babies in seventy-six good homes. The babies were judged normal by physical and developmental examinations and the homes lacked any of the undesirable factors previously mentioned. In sixteen instances, a questionable situation had been set up; usually "overplacements" such as described before. In eight cases the situation was so poor that we felt it should be terminated. Our advice was followed in two out of the eight cases.

The figures are compared in Table I.

TABLE I

RESULTS	TYPE OF PLACEMENT	
	% INDEPENDENT	% AGENCY
Good	46	76
Questionable	26	16
Bad	28	8

The time element is of great importance. In favor of the independent adoption are the early placements which presumably promote better emotional and personality development in the children. Of 100 infants placed independently, seventy-nine were under 3 months of age. Of 100 infants placed by agencies, only fourteen were under 3 months of age; before the agencies approached the seventy-nine figure, some of the children were 18 months old. Practically all of the 100 independent babies were placed before they were a year old. The agencies did not approach this score until some of the children were 2 years old. Table II summarizes these comparisons.

TABLE II

AGE OF PLACEMENT	TYPE OF PLACEMENT	
	% INDEPENDENT	% AGENCY
Under 1 month	61	10
Under 3 months	79	14
Under 6 months	83	33
Under 1 year	90	61
Under 1½ years	97	77
Under 2 years	99	90
Under 3 years	100	100

THE INDEPENDENT ADOPTION

If agency placements are so much better, then why do independent placements occur? There are many and good reasons such as ignorance of the value of the agencies, and the naive assumption that any person who wants to adopt a baby is fit to do so. But the principal reason is because the agencies are not doing a big enough job or a fast enough job, and they handle only a fraction of all the adoption situations. They handle that fraction well, but they do not and, as they are now constituted, cannot cover the whole field. In Massachusetts less than 10 per cent of adoptions are placed through agency supervision. In Connecticut for the year 1946, only 20 per cent were agency adoptions.

Independent adoptive parents are either uninformed about the risk of adoption, or they have been refused by an agency; some for good reason, some for insufficient reasons. But they still want a baby, and if the agency will not help them, they help themselves; or they are the people who have been accepted by an agency, have waited and waited, sometimes for years, they grow desperate, hear of a child and take him in their desperation. The urge of the childless who want to adopt is an almost irresistible force.

Independent placements entail a far greater risk, both to the child and to

the adopting parents. The advantages to the parent are that they can get babies this way, and they can get very young babies. The only advantage to the infant is that he is placed early and thus spared possible institutional placement for long periods, or the possible necessity of making adjustments to a series of foster homes. The advantages to the natural mother are that she is relieved of the responsibility of her child, quickly, cheaply, and easily. These are some of the reasons why independent placements are made, risk or no risk.

ADOPTION RISKS

Adopting parents of very young children will vow that the child's deficiencies will make no difference to them, but all too often when the child is older, they admit, "I didn't know what I was saying—what it would mean. Don't ever believe an adopting parent again, who says that," etc. The attitude changes in spite of the best of intentions. Anyone who has any concept of the enormity of the tragedy to parents of a mentally defective child would do whatever he could to protect a family from entering into such a situation.

There have been sufficient studies of the causes of delinquency and criminality showing what a vicious environment can do to personality and character development to warrant our never placing a child in a pathological home environment. Thus the adoption situation does endanger the child and he should be protected. He is a helpless pawn in independent adoptions. His feelings, his needs, his rights are hardly considered. The natural mother is protecting her good name, the doctor is doing his patient a favor, the adopting parents are fulfilling their desires, but what about the baby who cannot speak or act for himself? He needs at least an escape mechanism. The need for such is very great in independent adoptions where the placements are made comparatively at haphazard.

PROTECTIONS IN ADOPTIONS

The tools we have to work with, in our effort to protect the child, are the social workers' investigations which assess the value of the home for the child; the appraisal of the child and his background by the doctor and psychologist, which assesses the child's potentialities and his needs; and the probationary period which gives the worker and the physician time to make their studies, to see the home and the child together, and to make their recommendations. But if the probationary period is observed only in the breach, and the law permits this, and the investigation is dispensed with as just a nuisance, and the law permits this under certain conditions, we are depriving the child of his only protections. Or if we solemnly observe the probationary period, all 365 days of it, and then proceed with the consummation of the adoption, even though the situation is bad, we are making a meaningless gesture which protects no one.

The attempt of the present (Connecticut) law to control independent placements has controlled very little. The placements go on, and the adoptions are legalized, good or bad. Actually, the law provides no mechanism for removing a child from an undesirable home unless there is outright physical abuse or neglect, when the

humane society may step in. Nor does it make provision for removing a baby who is a poor adoption risk from good parents who love him, however misguidedly, and who refuse, however blindly, to see his defects.

SUMMARY

1. The present study shows that the social agencies do better adoption placements than does the well-intentioned or expedient laity.

2. Agency adoption placements are well done, on the whole, but they do not place enough babies, they do not satisfy enough adopting parents, and they work too slowly. Independent placements will continue as long as the agencies operate as they do now, which will certainly be until they have much more money and many more workers.

3. The probationary period should be, among other things, an escape clause. It should be implemented not only by the power to remove the child from the home, but by the courage to do so when necessary in the child's behalf, over the protests of the adopting parents if need be.

4. Our efforts must continue to educate the public, which will include potential adopting parents; lay persons who tend to become involved in arranging independent placements; the legislators who frame our laws; and the courts which render decisions on each adoption situation. Thus there will be a wider understanding of the great risks involved and of what constitutes good, safe, and decent practice.

5. The alternative to a bad adoption placement is not homelessness or the orphanage but a good placement.

EXPERIENCES WITH AN ELECTIVE ROOMING-IN PROGRAM*

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DURING the past few years several medical centers throughout the country have inaugurated the rooming-in plan of neonatal care. This has varied from a small, carefully supervised unit, where a long-term study of the early mother-child relationship is being made,[1] to a large-scale plan compulsory for all ward patients.[2] More recently, another large series, obligatory for both private and ward patients, has been reported.[3]

We believe that a report of our experiences at St. Louis Maternity Hospital may be of value, not only because of a quickening of interest in the plan in both professional and lay minds, but also because in our institution the program is not only entirely voluntary but has made its greatest appeal to private patients. In the twenty-month period from November, 1948, to July, 1950, 522 of our mothers have elected to room-in their babies. These are distributed as follows: Private White, 422; Ward White, 67; Ward Negro, 33.

Our experience with rooming-in began late in 1948, the result of a combined pediatric-nursing-obstetric desire to provide for interested mothers a more flexible type of neonatal care than that permitted by the centralized nursery. We were motivated then more by a wish to better the psychologic relationships between the mother and her newborn infant than by a need for the control of nursery infections. We wished to test our fundamental conviction that it is possible for mothers to participate in a rational and flexible neonatal program without architectural changes, additions of nursing personnel, and without psychiatric help, but rather as a part of a well integrated pediatric-obstetric partnership.

The psychologic basis for rooming-in has been well discussed by such qualified authorities as Jackson,[4, 5] Moloney,[6] and others. Briefly, its main tenets are as follows: (1) Fostering, from the beginning, a warm, permissive mother-child relationship, regardless of the multiparity of the mother; (2) providing a flexible feeding and sleeping routine suited to the needs of the individual infant; (3) giving the primiparous mother genuine practice in "mothercraft" so that she leaves the hospital confident and assured; (4) encouraging successful breast feeding.

Rooming-in as a major factor in the control of neonatal infection is a very real although less familiar aspect, but one which is gaining increased recog-

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*Miss Ann Campbell, Superintendent of Nurses, is due full credit for her active participation in organizing the rooming-in plan at St. Louis Maternity Hospital. The assistance of Miss Ruby Burdette and Miss Margaret Wooley, nursing supervisors working especially closely with the program, is also deeply appreciated. The cooperation of Miss Grace Huey, Superintendent, and of members of both obstetric and pediatric staffs is gratefully acknowledged.

†Fellow of the American College of Physicians during a portion of this study.

nition. Montgomery[7] and his group have particularly emphasized this advantage with recent support from McBryde and Davison.[3] Certainly the rigid principles of centralized nursery care with which profession and public have been so heavily indoctrinated over the past thirty-five years have proved singularly inadequate during the shifting and crowding of the war years. The evils of overcrowding and understaffing have indeed become so chronic that they are now taken for granted, and with the overwhelming shift toward hospital deliveries in urban centers, are unlikely to be ameliorated without extensive new building. Few institutions are capable of providing the facilities of space and personnel recommended by the American Academy of Pediatrics and the Children's Bureau.[8] In 1948, as experienced a pediatrist as Powers stated emphatically that ". . . I venture to predict that the rooming-in plan will prove to be safer than any other hospital arrangement for the care of the newborn."[9]

Although our hospital is not as well suited to the plan, architecturally speaking, as many others, we were unable to contemplate any structural changes. Because there are probably many other institutions which are hesitating to consider a rooming-in plan because of unfavorable architecture, the St. Louis Maternity Hospital will be described in some detail. The hospital is a T-shaped building, four floors of which are devoted to obstetrical patients. Two of these are for private white patients, one for ward white patients, and one for ward Negro patients. (Fig. 1.) On all these floors the central nursery is located slightly off-center of the long arm of the T, and hence the babies are not visible from the nursing stations which are located at the junction of the long and short arms of the T. Rooms and wards are similarly removed from the nursing stations, so that in order to check on patient or infant it is necessary to enter the particular room or ward. Thus the usual ward traffic of nurses, medical students, and house staff does not serve the rooming-in plan by providing casual observation. On the private floors

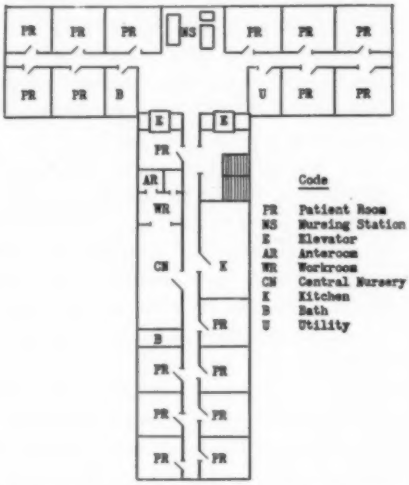

Fig. 1.—Diagram of plan of private obstetric floors at St. Louis Maternity Hospital.

there are both single and double rooms, some of which are equipped with lavatory facilities while others are not. Patients with the latter type of accommodation usually have a bathroom accessible within a short distance. All these rooms were originally designed to house only one patient, so that when occupied by two mothers, two infants, and the usual amount of furniture, radiators, and the like, the rooms are not exactly spacious. The

ward floors consist of two nine-bed wards and two four-bed wards each, with relatively accessible lavatories.

There is no way in which restless babies can be moved into an adjoining room and still remain under the mothers' observation. The only available space is a small room off the central nursery used as an examining room by pediatricians during the daytime. Since these rooms are not used at night, occasionally babies have been moved into these anterooms for a few hours during the night. As yet we have not returned babies to the congregate nursery once they have roomed-in. It is easily seen that our hospital, although modern, well equipped, and pleasantly decorated, is not ideally suited to the rooming-in plan. That we have found it adaptable and practical should, we hope, prove encouraging to others.

The question which is most frequently asked after "Don't the mothers get too tired?" is "Doesn't the plan take a lot more nurses?" Our answer is that while extra nursing is not required, a different type of nursing is necessary. By a different type of nursing we do not mean a redistribution of nursing care but rather that the average floor nurse is called upon to teach and to demonstrate and also to use considerable judgment and initiative. The need for a special nursing supervisor whose main duty is the overseeing and support of the "roomers-in" depends largely on the temper and adaptability of the regular nursing staff.

Under the rigid system of congregate nursery care there are few nurse-mother-infant situations to be met beyond getting the infant on breast. Interpretations of infant behavior are oversimplified and often wholly inaccurate. Crying, for example, is usually explained as a manifestation of temper, early "spoiling," or as a necessary concomitant of lung expansion. It has been easy to assume an attitude of lofty superiority which intimates not only that the baby "belongs" to the nursery rather than to the mother, but also that the mother is preternaturally a witless individual best kept in ignorance (until she goes home!). Thus a right-about-face in attitude has been necessary—the nurse must consider each baby as an individual, each mother likewise, to be supported and helped as occasion arises rather than dealt with on assembly line principles. It is a truism that teaching the novice is harder than doing the task oneself and that intelligent listening is harder than talking!

This change of pace has been a difficult one for many of our nurses, and the adjustment of necessity has been gradual. One of the very best features of the program is the genuine though generally unstudied "humanizing" of the hospital since the inauguration of the plan. Patients who have returned recently for a subsequent baby after an interval of a few years have remarked, "This seems like a different hospital; everybody is so nice!" Naturally this harmonious relationship is of mutual benefit. Parenthetically, many of the nurses who were the least enthusiastic to begin with are now our staunchest supporters.

Unavoidably, during the first few months many of our patients became aware of rooming-in only following

their delivery. After the plan gained initial momentum, news about it spread quickly. A few months ago a statement about its availability was added to the general information about the hospital which is given the patient when she makes her reservation. Ideally, the plan is discussed with the patient by her obstetrician during her pregnancy, so that she is thoroughly familiar with its aims well before the arrival of the baby. We find that mothers prepared in this way seem to enjoy the plan more completely and find it more deeply satisfying than those who happen on it. Patients who are essentially much interested in the program but whose obstetricians regard it as a pediatric foible sometimes experience a certain degree of conflict. This is not surprising when one considers the varying philosophies of a large obstetric staff. An excellent substitute for prenatal preparation by the obstetrician is a similar discussion with a qualified member of the nursing staff.

It has been possible to provide rooming-in only for ambulatory mothers. Fortunately, most of our patients enjoy early ambulation, although there are some who do not. Inasmuch as considerable extra nursing personnel would be required were the plan extended to bed patients and particularly inasmuch as we are strongly opposed to making any extra charge for rooming-in, this step has not proved feasible. Also, without special swing-over cribs, care of the infant can indeed prove tiring to the mother who must remain in bed.

Because the care of the baby is almost entirely up to the mother once he is roomed-in, this is not usually done until the third or fourth postpartum day, occasionally even later. Since the average hospital stay in our institution is ten days, the mother nearly always has a full week of experience with the plan. There are arguments both for and against this relatively late start. In its favor is the fact that the mother is always ambulatory by this time, has regained considerable strength, feels quite well, and may even be getting a little bored or homesick. The infant, too, has by this time gotten over any preliminary sleepiness, excessive mucus, and other symptoms characteristic of many newborn infants—insignificant enough to the old hand but terrifying to a new mother. Against it is the fact that the baby often moves in with the mother at the very period when he is notoriously most demanding. Our experience is similar to that of Frank,[10] Escalona,[11] and others that on the fourth or fifth day the average infant wants to feed between twelve and fifteen times, or even oftener. In spite of anticipation and reassurance, this may prove not only genuinely fatiguing to the mother, but may make her at once suspicious of the demand feeding schedule. If she has had twenty-four to forty-eight hours of a fairly quiet, easily satisfied infant, she is more amenable to the suggestion that this less agreeable behavior is a temporary phase.

Occasionally, the obstetrician, pediatrician, or the mother will want to "put the baby in for the last day or two." Although the mother does learn something about the actual mechanics of handling the baby by this technique, we are not in favor of this last minute type of rooming-in. Regardless of the

baby's behavior, the patient is much more wakeful the first night the baby spends with her, and if this is the night before discharge, she certainly may go home somewhat weary, supporting the contention that rooming-in is bound to be a tiring affair.

Prenatally, if possible, or soon after delivery, the mother who elects rooming-in receives some reading material discussing the general philosophy of the plan, along with such topics as the basic needs of the newborn infant, demand feeding, crying, sleeping, sleeping positions, and the like. This printed information seems to reinforce verbal conferences and discussions though is in no way a substitute for them. A considerable effort has been expended to make this material positive in its approach rather than negative or threatening.

When the baby is moved in, the first instructions and demonstrations of care and handling are given by a nursing supervisor. Following this the floor nurses take over, treating mother and baby as a unit. Babies are weighed daily and temperatures recorded twice daily. Behavior of infants is noted along with other nursing data in the "report" given each shift of nurses as it comes on duty.

Breast feeding is encouraged and is warmly supported by our nursing staff, who are thoroughly familiar with the techniques likely to make for success. In general, we have no more trouble with the nipples of mothers who are nursing their infants on demand (with consequent more minutes of sucking time daily) than those on a regular schedule. This seems to support the belief that the frequency of suckling has less to do with sore nipples than the type of sucking. A frantic infant, consumed with rage and hunger after enforced waiting, often traumatizes the nipple in the first few minutes of ferocious sucking and chewing. The use of a nipple shield as a temporary measure also may afford relief to the mother and satisfaction to the infant.

We certainly do not feel, however, that breast feeding is a prerequisite to successful rooming-in and suggest that it is unfair to deny the satisfactions of the plan to mothers and their infants for whom breast feeding may not prove feasible. The sense of guilt and failure consequent to such a denial could be exceedingly traumatic.

We have allocated a section of the iceboxes which are kept in the kitchen of each floor for nursery formulas, so that it is accessible to the mother at all times. Recently we have added several inexpensive individual bottle warmers to our equipment, so that there is no delay in this respect if the nursery attendant is busy elsewhere. We are now using cross-cut nipples on all nursing bottles and find that nipple problems (clogging, rate of flow) have virtually disappeared. Soft rubber premature type nipples are available for babies who need them.

One of the great advantages of breast feeding is admittedly that the mother is unable to see how much the baby has taken, so that he is likely to be allowed to continue to suckle as long as he wishes, whereas an empty bottle is quickly taken away from the formula fed baby. Yet the sucking desires of the neonate are tremendous, and undoubtedly the failure to satisfy

this need accounts for much of the bedlam accepted as natural in the congregate nursery. To this end we have made increasing use of the dry nipple or pacifier[12] (an ordinary nipple stuffed with sterile cotton). It is striking to see how much of the restlessness and crying of the newborn infant can be eliminated by the addition of this one element to the armamentarium of the flexible schedule. The truly hungry baby will have nothing to do with the pacifier, rejecting it immediately. Similarly, the satiated infant who yet remains wakeful and restless will accept it with enthusiasm, settling down to a period of contented sucking which may last only a few seconds, or he may continue in a trancelike state for some time before sleep overtakes him.

Fear of airswallowing, initiating colic, and the like have proved groundless. The nipple may be attached to a small nursing bottle, a #7 Lepage's mucilage bottle, or need not be anchored to a bottle. The dry nipple may also prove helpful with the breast-fed infants if the mother is having some temporary nipple distress. Another practice which has proved most useful in calming the restless infant is the tight swaddling of the baby in a light blanket, placing the extremities in the fetal position and then laying the baby prone with the head turned to the side. If this is done, the mother should be warned that the desire of the infant for swaddling does not last much over the neonatal period, after which time he will strongly resent any such restraints.

In addition to the nursing staff, advice and help are given by the pediatric house staff, consisting of the intern and assistant resident assigned to the newborn service. Our second-year men have thus had previous experience with the plan. For the intern, however, the experience may prove highly instructive since it is surprising how much of our pediatric teaching either still ignores the flexible type of infant care, or merely gives lip-service to it with very little know-how. For the first eight months of the program each rooming-in mother was interviewed daily by me, but this could not be continued indefinitely. A feeling of continuity is very helpful to the mother, but there is no reason why this cannot be given either by a capable nursing supervisor or by well-indoctrinated house officers. The private pediatrician can, of course, play a major role in the program, but it is unusual for an attending pediatrician to be able to spend the time with the mother that the plan demands.

The pediatric staff has been well satisfied with the progress of the babies on rooming-in. Like other centers, we have seen no case of significant respiratory, gastrointestinal, or skin infection. Weight gains are not only satisfactory but occasionally impressive, at times going "off the top" of the graphic sheet. With the exception of the fourth and fifth days of life, rooming-in babies do very little crying. Even at this time it can ordinarily be kept within bounds by resourceful supervision and if the mother does not become too upset. The contentment of the babies continues to surprise the uninitiated. One learns that although the baby does "set his own schedule" this is an everchanging one. The baby who nurses every one and one-half to two hours on the fifth day is likely to have many four- or five-hour intervals by the tenth. The number of infants who

prefer approximately a three-hour interval to any other raises a real question as to the desirability of the four-hour schedule which has been accepted as gospel for so many years.

The majority of our patients have declared themselves enthusiastically in favor of the plan. We are now sending out questionnaires to these first 522 patients to see whether this reaction was lasting. Not infrequently, certain mothers (especially those whose prenatal preparation has been sketchy) have their doubts along about the fourth or fifth day as to the value of rooming-in versus rest. This feeling is usually replaced in a few more days by a sense of calmness and confidence. At this time the mother is likely to recall her earlier turmoil with amusement, and such remarks as "Of course that night was awful, but if it had happened to me after I had gone home I should have gone out of my mind. Now I'm used to him and know what to expect" are common.

As mentioned earlier, the mother who is well prepared by her obstetrician and who has her own convictions about the desirability of rooming-in usually has very little trouble. The mutual satisfaction of herself and her baby readily compensates for minor and transitory inconveniences. Many participants have said they are more rested than with the old type of puerperal care. This is for two reasons, first that they are assured of the baby's comfort and welfare when under their own supervision, and second, that since mothers too are "on demand" they are relatively undisturbed by hospital routines.

We are unequivocally opposed, however, to the use of rooming-in as an obligatory method of neonatal care at the present time, at least for the private patient. The only exception would be in the presence of newborn diarrhea or other infection rendering the central nursery a menace. Neither the obstetric profession nor the lay public, at least in our locality, is ready for any such step.

There are some mothers for whom rooming-in will probably never be right, just as there are some for whom demand feeding is not the best policy. There are some patients who are so worried and tense (whether in relation to the baby or not) and who have been so exhausted emotionally by the events of pregnancy and delivery that they are simply unable to withstand the demands of the rooming-in program, both physically and emotionally. If the plan is forced on such an individual, she is likely to handle the situation with a tension and anxiety, if not actual rejection, that could traumatize the baby far more severely than ordinary nursery care. As Escalona[11] states, "We may be doing the baby a doubtful service by exposing him to continued and extensive contact with such a mother." There is also the highly intelligent mother who might be most interested in the plan if presented to her correctly but who nonetheless will be bitter and uncooperative if it is thrust on her willy-nilly. Rooming-in should remain an elective privilege, not an order.

We do not pretend that the plan will correct all the psychiatric ills with which our world is presently afflicted. We do agree, however, with Jackson,[12] that for the mildly inadequate mother it "directs attention to the important psychiatric considera-

tion that the child's freedom to learn and his capacity for self-discipline is rooted in his infantile and early childhood satisfactions," and that for the adequate mother, rooming-in is "the ideal opportunity for starting a happy relationship."

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THE ASTORIA PLAN: A DECADE OF PROGRESS

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HISTORICAL BACKGROUND

IT MAY be well to cite a few historical facts in order to give the background and the evolution of School Health Services in the United States.

There is nothing "new dealish" or "fair dealish" about health services for children in schools. It was inaugurated about fifty years ago, though some phase of health service was offered in schools almost 100 years ago, such as sanitary inspections, i.e., environmental sanitation and compulsory vaccinations in some areas.

The first organized School Health Service began in Boston in 1894 under the leadership of Dr. Durgin, the health officer at that time. It was, however, a direct result of demands from parents and teachers and civic leaders.

The first School Health Service in New York City was established in 1897. About 150 part-time physicians were appointed by the Board of Health. Their chief function was to visit schools each morning for about one hour per day to examine children for evidence of contagion.

New York City, under the urging of the great nursing and social service pioneer, Lillian Wald, who demonstrated the value of the nurse's function in schools in a pilot study, was the first city to introduce public health nurses in the schools in 1902.

Most school health services had their impetus with the exclusion for contagion as their focal point, for they were mainly concerned then with the control of communicable diseases, and rightly so. The services were launched during an era when great epidemics were prevalent and mass immunization was almost totally unknown. It was, therefore, at the beginning merely an *inspection* and *screening* service.

With the advancement of medical and public health knowledge and new discoveries, and the consequent control of communicable diseases, the "inspection service" gave way to a "case-finding service."

In 1905 it was decided in New York City to examine *each* child for the presence of defects, and to attempt their possible correction. The nurses did screenings in the classroom, and the physicians saw the children referred to them.

About 72 per cent of all children thus examined were found to be in need of some medical care. As is the practice today, the children in need of care were referred to their own physicians or to free clinics, if they were unable to pay for private medical care.

The emphasis by 1911 was on physical examination while the nurse did the inspections for contagion, thus allowing the physician more time for the examinations. Many periodic physical examinations were done, and serious attempts were made to correct the defects found. The emphasis was on the find-

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ing of defects and not on the *whole child as an individual.* In the constant search for defects, the child was almost lost in the shuffle.

The school health service in New York City attempted periodically evaluation studies, appraisals, and self-criticisms with only one objective in view—how better to serve the child in the schools.

In 1925 an evaluation study revealed that less than 22 per cent of all defects found were corrected. The evaluation study of 1933, "Pathway to Correction," which was a study to determine why physical defects went uncorrected, showed a lack of coordination between the education staff and the Health Department, and the need for an appraisal of available clinical facilities. It was obvious that additional critical evaluation studies were needed.

The Astoria Health Demonstration Study was a culmination of a series of previous studies which were inaugurated from time to time with a view to solving some of the existing difficulties, and determining how to improve the services to children in the schools.

Pediatricians, educators, and public health workers realized the inadequacy of primarily doing *routine* annual physical examinations without proper guidance to parents, teachers, and to the individual child. They also realized that it was the child as a *whole* and his total personality which must be studied and investigated, and not merely the defects which were found and in the main went uncorrected. The study bears its name from the geographical location where it was first launched. It started in July, 1936, and was intensively carried on till June, 1940. In 1941 the plan was put into operation on a city-wide basis in New York City.

ASTORIA PLAN

The Astoria Plan[1] aims to concentrate school health services on children most in need of care, and not merely on doing routine annual health examinations. Only new admissions are examined routinely. It has been amply shown that the routine rapid examination of all school children year after year with the findings of the same physical defects, with no adequate follow-up and correction, without guidance to the individual child, and without proper interpretation to parents is not productive of good health services to children in schools. The Astoria Plan also evolved the philosophy and basic concept that the physician, nurse, teacher, and parent must act as a well coordinated team in unison, each contributing his or her share in the best interests of the individual child.

Parental Participation.—Parents are actively urged to be present at the time of the examination of new admissions or special referrals, since individual health guidance to parent and child is a major concept of the Astoria Plan. No examination is meaningful nor worth the effort unless the parent is present to answer questions, to give a detailed history, and to receive instructions from the physician and nurse regarding recommendations and follow-up.

The health examination thus serves also as a health education experience for the parent and child.

Teacher-Nurse Conference.—One of the most important and most productive aspects of the Astoria Plan is the teacher-nurse conference, for it is the most important case-finding device for

children with health problems who are in need of further investigation or care. The teacher and nurse work very closely together to accomplish this aim.

Once or twice yearly, by appointment, a teacher-nurse conference is held in the classroom. In this conference, the health records of each child are jointly reviewed, and all problems relating to the health of the child are discussed. There is a free interchange of opinion between nurse and teacher regarding the latter's observations.

It should be emphasized that referrals by teachers to the nurse of children with possible health problems are not limited solely to the scheduled teacher-nurse conference, but may occur at any time whenever the teacher believes there is a need for it.

Records.—No service can function effectively without adequate records and good bookkeeping. The Astoria Plan was cognizant of this basic principle, and made the necessary provisions. For each child in school, two continuous and cumulative records are kept: one, the "Pupil's Health Card," is held by the teacher and on it she records periodically her observations of the health behavior of the child concerned; the other record, the "Medical Record," is kept in the medical room, filed by the nurse, and contains the continuous medical history and health findings of the child, all his contacts, and follow-up by the School Health Service. Both records are used during the teacher-nurse conference and whenever the physician examines or inspects the child. These records follow the child throughout his school career. They are transferred at the time of his graduation from the elementary to the secondary school in which he enrolls.

It is on the basis of observations indicated on these records, and their periodic review, that a child with a health problem is selected for referral to the school physician for either a "screening" or "specially referred" examination.

A screening is a rapid review by the school physician to determine the possible existence of a health problem. A special referral requires a complete examination with a parent present and more intensive follow-up.

Through the medium of screenings and special referrals, children who present significant health problems are referred to treatment agencies, their private physicians, or clinics. Needless referrals are scrupulously avoided.

Follow-up.—While case finding through the media just enumerated is presumably efficient, its usefulness would be of no avail if an effective follow-up program were not available. The public health nurse in the school is the most important person in this area, for she is the chief overseer in the follow-up of recommendations. She devotes a large part of her time to seeing that "things get done."

The nurse not only acts as an advisor to parents, teachers, and children, but she actively assists the parent in promptly securing the necessary follow-up. The parent is not only advised of the physician's findings and recommendations, but is strongly urged to institute prompt correction of any remediable defects.

Referrals to treatment agencies are made with a detailed statement of conditions found at the time of the examinations, and requests for opinion and recommendations from the treatment agency are made. The private physician or treatment agency is asked to

fill out the form in detail so that the school health service will be able to follow up the private physician's recommendations and refer the child back to him for further care whenever he indicates a need for such referral.

Consultation and Other Services.—School Health Services do *not* include treatment. They are limited to case finding, diagnosis, health education, and follow-up of the individual child in need of treatment to insure that such treatment is obtained as rapidly as possible.

Some consultation and diagnostic services, such as cardiac, orthopedic, and eye, are available for school children; ear diagnostic services will soon be included. These diagnostic and classification services are manned by recognized and qualified specialists in the respective fields, and may be utilized for referral of a child in school by the private physician or the school physician.

Staff—Qualified Personnel.—In order for the Astoria Plan to operate effectively, a well-coordinated team is essential. Since no chain is stronger than its weakest link, all members of the team must be well qualified and specially trained to carry out the program.

Training Program for Staff.—School physicians are *practicing physicians* employed on a part-time basis, and they are selected by the Department of Health on the basis of qualifications, previous training, interest, and experience. Prior to their appointment, they are given a six-week intensive indoctrination *"pre-service" training course* by a select faculty consisting of physicians skilled in school health administration and practices, and educators specializing in health education and child welfare. The course aims to acquaint the prospective school physician with the problems, aims, objectives, philosophies, concepts, methods of administration, and health records of the School Health Service.

The school nurse is likewise selected because of her training and experience, and in addition receives *in-service training* in public health practices and techniques as they relate to school health.

In-service training for the entire staff in order to promote their professional growth and development is offered throughout the year by recognized national authorities in the fields of Growth and Development, Mental Hygiene, Public Health, Nutrition, and other related subjects.

Teaching the Teachers.—The importance of the teacher in the team and the Astoria Plan cannot be over-emphasized. The teacher is the most strategic person in the case finding of the child in need of medical care and supervision. The teacher is in daily contact with the child and spends more time with him than either the nurse or physician. In addition, she is also more detached than the parent, and thus has a rare opportunity to observe the child and his progress, to note any deviation from good health, and to refer such a child for further investigation. Since the initial discovery of children with health problems in the Astoria Plan depends on the astute observations of the teacher, it is necessary to teach the teacher what to look for.

It was, therefore, realized that it is not sufficient to merely give alertness courses periodically to teachers on health conditions, but that it would be far more profitable to start orienting

the prospective teachers in the teacher-training schools early in their careers.

With that aim in view, a pilot study was made last year with senior students at Queens College. Student teachers who were assigned to New York City public schools were given an opportunity to observe school health services in action, i.e., at least one doctor session and one or two teacher-nurse conferences during her assignment to the school as a trainee teacher.

All the trainee teachers were extremely enthusiastic about this observation and indoctrination period, and it is planned to extend this training to include a home visit by the student teacher with the nurse. Each student will have a conference with the public health nurse in the school following her observation period.

It is planned to extend the training to the other teacher training colleges in the city.

In addition to the demonstration periods, students will visit the district health centers and attempts will be made to explain to the students the function of the health center and its relation to the community and the special services available for children of school age.

Members of the school health staff have also offered their services to the colleges as consultants on course content and planning as related to Health Department activities.

The student teacher health training program has wide implications and should prove of great value in making future teachers more health conscious and ultimately better observers and case finders.

Private Physician.—In the Astoria Plan, as practiced in New York City, the School Health Service relies heavily on the private physician. It is the private physician who examines approximately 50 per cent of all new admissions, and thus he is a very important person in case finding and health counseling, in addition to treating children who are in need of care and treatment.

It is, therefore, extremely important that the physician should not look upon the health appraisal as a mere routine formality, but as a rare opportunity for preventive medicine at its best. The private physician, because of his knowledge of the family background and history, growth, and development, is particularly fitted to properly appraise the child's health status and make the necessary recommendations.

Administration and Implementation of School Health Service Plan.—Every plan, regardless of how perfectly conceived, needs implementation and execution. However skilled physicians, public health nurses, and other members of the team may be in school health practices, the Astoria Plan, or any plan or service for that matter, cannot function effectively without a closely coordinated administrative plan and supervision. New York City was indeed fortunate in having Drs. Leona Baumgartner and Robert W. Culbert at the helm to implement and execute the plan.

Coordinating Council.—Throughout the years there has always been a fine spirit of cooperation and fine working relationship between the school health services and the various divisions of the Board of Education. In 1946 a Coordinating Council on School Health was formed in which the top administrative officers of both services meet once each month throughout the school

year to discuss mutual problems of administrative policies and to plan their solution. No policy by either department is thus unilaterally formulated without the full knowledge and consent of the other.

Local school health councils for mutual cooperation have also been formed. Thus there are cooperative efforts at various levels of administration working effectively so that the child in school may receive the best health supervision and guidance which is rightfully his.

Effectiveness of the Astoria Plan.—In the main, the Astoria Plan has accomplished its goal. It has withstood the test of time and weathered an aftermath of a depression and a World War with its resultant dislocations and adverse effect on the staff. The plan has been widely accepted throughout the United States and even abroad. In New York City since the Astoria Plan was instituted the services to the child in school have tremendously improved, as follows:

1. From 30 per cent of parents present at time of examination in the pre-Astoria days to over 75 per cent since.
2. Better individual health guidance.
3. Better follow-up and more prompt correction of defects found.
4. About 95 per cent of the entire case load completed every year.
5. Private physicians' examinations increased from 14 per cent in 1936 to over 50 per cent in 1949.
6. Better qualified personnel.
7. Better health records and all-around better bookkeeping.
8. Better coordination of services between agencies involved.

Thus, the Astoria Plan in New York City has worked very effectively. However, there have been very few and limited evaluation studies of the effectiveness of the Astoria Plan.

Dr. Yankauer's study[2] in 1946, which was done on only 114 children and in one district, concluded that the Astoria Plan of School Health Service functioned satisfactorily in the schools surveyed. This, of course, was very limited in scope. Many more large-scale evaluations and continued critical studies are, therefore, needed to properly assess and evaluate the Astoria Plan in action.

LOOKING FORWARD AND PREDICTIONS OF THINGS TO COME

Is the Astoria Plan an ideal plan and here to stay? I believe definitely not. May I emphasize, however, that it is the best system yet devised, especially for a service with limited budget and personnel. I cannot refrain, however, from pointing out some inadequacies in it, and from making predictions that the Astoria Plan will some day, because of continuous evaluation studies and changing conditions, give way to another system which will make the Astoria Plan of today perhaps as outdated and obsolete as the Squad System of examinations of 1932.

May I also point out that any adverse criticism is *my own*, and not an official opinion of the Health Department.

The major inadequacy in the plan, as I see it, is that while it proclaims to give priority to children *most in need of it*, the primary selection of this important group is entrusted *entirely* to a group *not professionally qualified to do so*. It is true that the teacher consults with the nurse, who in turn refers the child selected by the teacher to the physician—who *is* qualified. But

how about the child in need of health supervision who is *not* picked up by the teacher?

We are not interested in finding children with major defects only, or with adverse conditions of long standing. The fact that a teacher could pick out a child as needing medical care would more likely than not mean an adverse condition of some duration.

How about the detection of early emotional disturbances which are so common, and which if undetected become aggravated and give rise to the major psychoses or neuroses of later life? The teacher, being professionally untrained, is far more likely to pick out a child with a major physical defect rather than a case in its incipiency which is more amenable to correction. Is it not more important to *maintain* an ideal state of health, including physical, mental, emotional, and social, than to treat an existing adverse condition of some duration?

Should priority be given to children with obvious defects rather than to the child who is just beginning to show evidence of poor health, whether physical or emotional, but can easily be restored to good health with a minimum degree of effort and expenditure?

A teacher, regardless of how keen an observer, is not qualified and, because of her other professional duties, is unable to pick out the numerous early cases in need of health supervision, and she should not be forced to be put in a key position as the discoverer of such children.

While it is true that routine rapid annual physical examinations with no emphasis on correction of defects are worthless, it is also true that one routine examination on admission only is *not* sufficient. All too many children in need of health guidance and supervision are entirely missed under the present plan in New York City, as witness the fact that only 80,000 screening examinations, and out of this number only 37,000 special referral examinations, result annually out of a total registration of about 900,000, a little over 4 per cent of the total registration.

Obviously there must be a far greater proportion of children in need of further health supervision. The discovery of children with physical and especially psychological problems is in direct ratio to the degree of effort and skill devoted to it. It is, therefore, unwise to rely so heavily on the teacher alone as a *case finder*. The teacher's special training, aptitudes, and skills should preferably be utilized in the areas of health education, general hygiene, and follow-up. I do not advocate exclusion of the teacher as an observer, but supplementing her. There is a need for at least two more routine examinations during the elementary school career.

In a cross sectional study[3] on the health status of children examined by school physicians in New York City in March, 1949, there were 11,171 defects recorded on 14,132 children. Of these, 5,202, or 46.6 per cent, of all defects were newly discovered during the study, while the new admission examinations constituted only 24.4 per cent of the total population under study. This finding implies that many adverse health conditions are not detected by the present method, and that more routine examinations are needed. More and better case finding media are also needed.

While, theoretically, the private physician should be in a better position

to assess the child's health status and to make the proper recommendations, for as mentioned before he knows the child's background, family, social history, growth and development, etc., in practice, however, it does not always work quite that way. A review of records on school children examined by private physicians will reveal that a surprisingly large number of children will be marked merely as "normal" though they present many obvious adverse conditions. The ratio of unnoted adverse conditions by the private physician is much higher than by the school physicians. There are several factors which may help to explain this discrepancy:

1. The average private physician is very busy.

2. He is still by virtue of present training and experience more interested in clinical findings and treatment, rather than in prevention or health supervision.

3. He looks upon the examination for admission to school as a mere formality.

4. He may yield to parents' requests not to mark child as having adverse conditions.

I am not advocating supplanting the private physician, but supplementing him. Let us have, by all means, more private physician examinations. But why should the rich be penalized? Why should not a child of better economic status receive the same privileges in the school as any other child? Full health supervision should be given to all children in all the schools. Children should be examined by their private physicians as often as possible, but not at the exclusion of health supervision by the school physician. All data obtained on a child should be utilized. A free exchange of ideas and opinions regarding the health status of a child between school physician and private physician is desirable. There should be good rapport and liaison between the school health service and the private physician, for everyone is working for the same objective—the health of the child in school.

PREDICTIONS OF THINGS TO COME

What I am about to predict may sound *visionary*, improbable, or at best *unrealistic*, especially in the face of the report from the American Academy of Pediatrics' Study of Child Health Services. The report discloses that more than 50 per cent of the counties in the United States had no system of medical examinations in their public elementary schools in 1946, and that over one-third had neither medical nor nursing services, and that a large part of the country had inadequate services.

I cannot refrain, however, from believing that what I predict will happen some day:

1. Full and adequate health supervision, physical, mental, emotional and social, including healthful and safe surroundings for all children in all schools.

2. In addition to present case finding media, additional and more accurate screening devices will be employed.

3. A greater understanding of the problems of impaired hearing, speech, reading, writing, and vision, their early discovery, treatment and prevention.

4. Greater emphasis on absences, their causes and prevention, and their utilization as a case finding medium, especially for children with rheumatic fever and rheumatic heart disease.

5. Greater emphasis will be paid to the discovery even of minor emotional disturbances, which if detected early may be easily corrected and thus prevent delinquency, and perhaps major psychosomatic ills in later life.

6. Greater emphasis on causes of accidents and their prevention.

7. Greater emphasis on the causes of truancy and its prevention.

8. More adequate psychotherapeutic facilities.

9. More adequate dental and nursing facilities.

10. Supervised and more adequate recreational facilities.

11. More attention focused on the emotional problems associated with handicapping conditions in children.

12. Greater acceptance and normalization of the handicapped child.

13. Normalization and admission to school of the epileptic, diabetic, and asthmatic child who is under treatment.

14. Greater emphasis on teaching teachers to become good observers.

15. More adequate diagnostic and consultation facilities.

16. Greater emphasis on nutrition and the early detection of children with nutritional inadequacies.

17. Greater emphasis on the importance and the quality of parent-child relationship. Greater emphasis and better understanding of the problems of adolescence and youth and their appropriate management.

18. Wider and more complete integration of school health services with community health services, including public and voluntary health agencies. Service rendered will be based on *needs* and *available facilities*.

19. More *active* participation of the *private physician* in the school health services. The private physician will be considered as *part of the team*.

20. A greater awareness of social medicine on the part of organized medicine and the individual practicing physician.

21. Closer coordination and interaction between health educators, school administrators, and health personnel.

22. The private physician will be better informed on aims and objectives of school health services. He will have a greater knowledge of basic principles of public health and preventive medicine and will be better suited to carry out his functions in the community of which the school is but a part.

23. The school physician will be considered as a specialist on a par with the other recognized specialists. His qualifications will include not only pediatrics or internal medicine, but graduate work in preventive medicine and public health, mental hygiene, nutrition, principles of education, school administration, and human relations. He will be a leader and abreast of latest discoveries in the fields of medicine and public health.

24. The school physician will be asked for consultation and advice regarding all health phases of children in school by the private physician.

25. He will be considered as a member of the organization staff of the school.

26. In addition to his present duties and functions as a counselor, consultant, and advisor to principals, teachers, nurses, parents, and children, he will visit classes periodically where he will have a rare opportunity to observe both the teacher and pupil and their behavior and reactions in the school environment.

27. The school physician will conduct periodic doctor-teacher conferences which will prove invaluable as a teaching medium for the teacher to help her become a better observer, and he will also be able to detect children in need of further investigation.

28. He will engage in more positive health education, including prevocational and vocational guidance.

29. He will be interested and actively participate in the instruction of health education, recreation, and physical education.

30. He will have periodic conferences with private physicians in the community relating to the health of the school age child under their care.

31. The school physician will consult periodically with the private physician or other treatment agency about the management and the total needs of the handicapped and the homebound child, and the child's complete rehabilitation.

32. Every school will have a doctor and nurse daily, at least part of the time.

33. Each child will be studied individually and will be afforded the greatest opportunity for the utilization of his fullest potentialities physically, mentally, emotionally, and socially.

34. There will be a shift in the emphasis on the part of the private physician and school physician from *case finding* to ideal health attainment, its continued maintenance and health promotion.

It is gratifying to point out, however, that whatever the plan, the primary purposes and functions of School Health Services from its inception have always been fundamental, basic, and clear—to serve at all times the best health interests of every child in the school.

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Case Reports

NEUROBLASTOMA SYMPATHETICUM WITH METASTASES

Report of a Case With Apparent Recovery

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NEUROBLASTOMA is a highly malignant tumor that metastasizes early and widely as is well-demonstrated in numerous published reports in which there were no recoveries.[1, 2, 3] Farber,[4, 5] however, was the first to point out that the prognosis in this type of tumor, while serious, is not always hopeless. Reports in the literature of recovery are few, and the possible mechanisms in such recovery as listed by Farber[4] are as follows:

1. The neuroblastoma may undergo spontaneous hemorrhage and necrosis and disappear without any treatment.

2. The neuroblastoma may undergo spontaneous maturation or metaplasia and become a benign ganglioneuroma. Cushing[6] reported this phenomen in a patient from whom he removed a ganglioneuroma from the paravertebral region at the level of the sixth dorsal vertebral body where ten years previously he has found a neuroblastoma. Chandler and Narcross[7] have reported two similar cases.

3. The neuroblastoma may be treated successfully by a combination of surgical removal of the tumor followed by irradiation. Lehman[8, 9] reported a case of neuroblastoma with recovery after surgical removal of the tumor, while Kerley[10] reported one five-year survival and one twelve-year survival. Farber[4] was the first to report the recovery in two patients who had liver metastases and in eight other patients without metastases who have remained alive and well for a number of years after surgical removal of the tumor.

The case to be reported here is one in which there were definite metastatic lesions in the liver, demonstrated during an exploratory laparotomy, and probable metastatic involvement of the skeletal system by x-ray. It was found impossible to remove the original tumor, and so the patient was treated with small doses of x-ray irradiation and with supportive therapy in the form of whole blood transfusions. This patient is still alive two years after the discovery of the tumor and has no apparent sign of the disease.

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CASE REPORT

G. S., a white male, was first seen on March 4, 1947, because of a mild upper respiratory infection and was found to have a mild otitis and pharyngitis. Physical examination was otherwise negative. The parents were healthy, and the pregnancy had been normal. Birth weight was 6 pounds, 7 ounces, and on feedings of evaporated milk supplemented with vitamins, his weight at 4 months of age was 13 pounds and his height 24½ inches. He was again observed a month later, at age 5 months, with a mild rhinitis but no other abnormality. Three weeks later, however, on April 28, 1947, he suddenly developed bilateral hemorrhages of the eyelids and, when examined, in addition to the periorbital ecchymoses, was found to be definitely anemic and to have a palpable mass in the upper right abdomen. This was firm, not too sharply outlined, but slightly movable, and appeared to be beneath the liver which was pushed somewhat upward and forward. On fluoroscopy, a radiopaque mass was seen in the right upper abdomen, and the right diaphragm was considerably higher than the left.

After admission to the St. Catherine's Hospital, Whiting, Ind., for

Fig. 1.—The baby as he appeared at time of the exploratory operation. Note the periorbital ecchymosis, bulbar conjunctival hemorrhage, and proptosis. (Photograph courtesy of Dr. John Keeley, Chicago, Ill.)

study, the following laboratory findings were obtained. Blood: hemoglobin 7.4 Gm., erythrocytes 3,040,000, platelets 60,800, leucocytes 7,500 with a differential of 1 basophile, 2 eosinophiles, 1 juvenile, 2 stab cells, 26 segmented cells, 68 lymphocytes, and 5 normoblasts per 100 leucocytes. Bleeding time was 11 minutes and clotting time 4½ minutes. Blood chemistry: nonprotein nitrogen 38 mg., chlorides 569 mg., total serum protein 6.6 Gm., with albumin 5.3 Gm. and globulin 1.3 Gm. per 100 c.c.

An intravenous pyelogram showed the right kidney pelvis much lower than the left, and x-rays revealed, in addition to the mass in the right upper quadrant noted on fluoroscopy, an area of localized rarefaction in the upper right humerus and a suggestion of similar areas in the skull. The patient was given three whole blood transfusions of 100 c.c. each while in the hospital and six deep x-ray treatments to the right kidney region in divided doses of 200 roentgens for a total of 1,200 roentgens. The patient was then transferred to Mercy Hospital in Chicago for surgical exploration. At this time, the periorbital and conjunctival hemorrhage and proptosis were rather marked (Fig. 1). The patient's abdomen was explored on May 24, 1947, by Dr. John Keeley, a member of the surgical staff of Mercy Hospital, and the liver was found to be extensively involved with nodular masses—some soft, some hard—which varied in color from light yellow to orange. Some were whitish in color. There were nodules up over the dome of the right lobe of the liver, and upon palpating the region of the right kidney, the lower and middle portions of the kidney were entirely normal. The upper portion of the kidney was in continuity with a retroperitoneal mass which seemed to come upward and anteriorly to involve the liver in a nodular manner. A biopsy wedge of the liver was taken. Microscopic examination of this tissue showed the liver to be involved by extensive tumor deposits of a neuroblastoma. The tumor revealed very well-defined rosette formation over wide areas, and elsewhere it grew in more solid or cordlike closely packed masses of cells in a fibrous stroma (Figs. 2 and 3). The patient was given two more blood transfusions of 120 c.c. each and was discharged to be followed at home. During the month of June, he was given five more sessions of x-ray therapy to the right kidney region for a total of 750 roentgen units. X-ray therapy was stopped because he developed a marked leucopenia and anemia. Also during this month he was given two blood transfusions of 120 c.c. each. The patient, however, seemed to be getting more marked proptosis, so that celluloid protective shields had to be constructed for his eyes. During the month of July, he was given two whole blood transfusions of 120 c.c., but his condition remained grave. He was seen again on Aug. 16, 1947, and, surprisingly enough, showed rather striking improvement. His weight was 15 pounds, 8 ounces. The mass in the right side of his abdomen was smaller, and the proptosis was not as marked. He showed no evidence of anemia. He

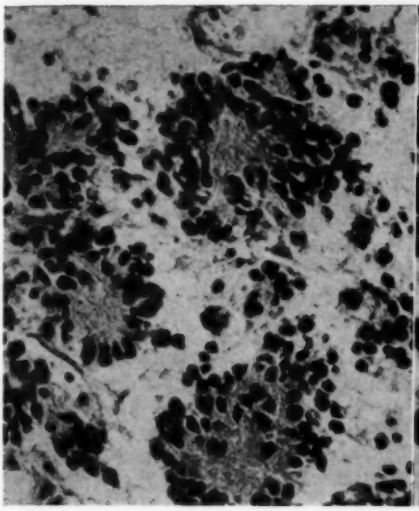

Fig. 2.

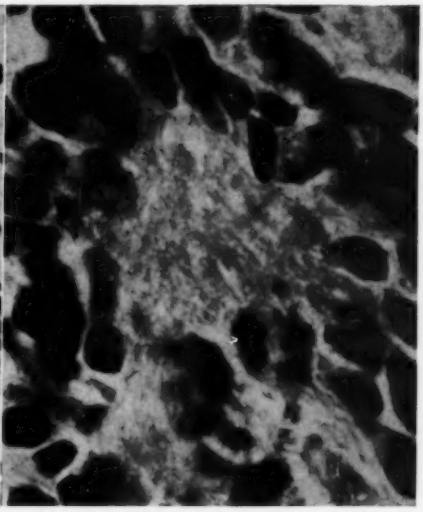

Fig. 3.

Fig. 2.—Position of the Kidneys in situ. Note size and proximity to one another. formation. Magnification power ×10.

Fig. 3.—Typical rosette formation of cells. Magnification power ×95.

was seen again one month later, and he had gained two pounds. The proptosis was very slight, and the mass in the right side of his abdomen was smaller. The patient was followed at periodic intervals and continued to show improvement, and when he was seen on Sept. 8, 1948, at 23 months of age, his weight was 25 pounds, and his height 34 inches (Fig. 4). At the time he showed no clinical evidence of the original tumor. His proptosis was absent as was the right-sided abdominal mass. X-rays of his skeletal system taken on Nov. 24, 1948, and Sept. 15, 1949, revealed no metastases. An examination of his peripheral blood was within normal limits.

It is difficult to explain the favorable outcome in this particular case. One might assume that the topical x-ray therapy which, although small in amount, produced necrosis and destruction of the tumor and possibly also that of the metastatic lesions in the liver. It would be extremely difficult to explain the disappearance of the metastatic lesions in the skeletal system and periorbital regions. Again, it is worthy of emphasis that the prognosis in this

Fig. 4.—The patient as he appeared on Sept. 8, 1948, at which time he showed no evidence of original tumor.

type of tumor is serious but by no means hopeless.

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THROMBOSIS OF THE INFERIOR VENA CAVA AND RENAL VEINS WITH HEMORRHAGIC RENAL INFARCTION IN INFANCY

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INTRODUCTION

HEMORRHAGIC infarction of the kidney usually is considered to be secondary to venous thrombosis and to be a rare lesion in newborn infants and in older children.[1] Renal thrombosis is extremely serious at any age, and in infants it is generally fatal. A review of the literature during the last three decades bears out the paucity of reports of hemorrhagic infarction of the kidney, associated with thrombosis of the renal vein, occurring as a complication of diarrhea of the newborn infant.[2] McClelland and Hughes[3] found only three cases of renal thrombosis with renal infarction from a review of 328 necropsies on infants. Of the 328 infants, thirty-one had clinically severe diarrhea. The three cases mentioned occurred among these thirty-one infants. In a study of 4,600 necropsies, Behr[4] located thirty-seven cases of thrombotic obstruction of one or both renal veins; however, in only three of these thirty-seven cases was there rapid obliteration of the renal veins with resulting hemorrhagic renal infarction. In 1934, Hepler[5] was able to collect only forty cases from the literature. Up to 1936, forty cases of renal thrombosis and infarction in infants and children had been studied at necropsy at the Babies' Hospital, New York.[6]

Despite the rarity of reports in our literature today, the older European literature contains a plethora of material on the subject. The first concise description of the condition was made by Rayer[7] as early as 1837. Bednar[8] and others [9, 10, 11] followed with contributions on this pathologic entity.

Usually it is believed that there is no preference for either side in the formation of renal vein thrombosis. The incidence is about equally distributed among males and females. Abeshouse's[12] study of 228 cases revealed the incidence to be greatest in infants less than 1 year of age. Of his cases, ninety-eight occurred in that age group.

An important factor of renal vein thrombosis in infants is severe diarrhea. However, there is usually an infection elsewhere in addition to that found in the gastrointestinal tract. The role of infection was first emphasized by Frühwald[13] as early as 1885. Subsequent investigations by Behr, Nordwall,[14] Oppenheim,[15] Petremand,[16] and others revealed that the renal thrombosis in these instances was associated with acute suppurative pyelonephritis secondary to enteritis. However, more recently, Morison[1] and McClelland and Hughes,[3] as well as Barenberg and his co-workers,[2] reported a total of seventeen cases of thrombosis with renal infarction which were not associated with acute suppurative pyelonephritis.

Several explanations have been advanced for the occurrence of renal thrombosis in infants with ileocolitis. Although no single acceptable explanation exists, some comment should be made on the pathogenesis. Formerly it was believed that all thrombi started from infection which was initiated by some degree of bacterial injury to the intima of the blood vessel. In some instances, however, mechanical, chemical, or toxic insult to the endothelium of the blood vessels may initiate thrombosis. Secondary factors which may exert an influence on the development of thrombi are changes in the velocity and direction of the blood flow, changes

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in the components of the blood, infections in the tissues in the vicinity of the blood vessel involved, dehydration, and angiospasm, as well as the predisposition of the newborn infant to venous thrombosis because of lowered pressure in the venous system, corresponding to shock, which is prevalent at birth.

The symptoms of renal thrombosis in newborn infants are the same as they are in adults; however, the infants are unable to complain of the severe flank pain described subjectively by adults. The outstanding symptoms in newborn infants are: progressive severe diarrhea followed by severe dehydration, palpable masses in the renal regions, which increase in size, edema, hematuria, albuminuria, and oliguria, followed almost invariably by anuria, shock, and death within a period of days. Campbell and Matthews[17] stated that the prognosis of this condition is exceedingly grave, and that more than 95 per cent of the infants with renal thrombosis die unless prompt surgical intervention is instituted.

Hypertension is a relatively rare finding in cases of thrombosis of the renal vein. A case of fatal hypertension due to bilateral thrombosis of the renal veins in a 12-year-old boy was reported by Perry and Taylor[18] in 1940. Three other cases in which renal infarction was considered to be a cause of hypertension in adults have been reported in the literature. Prinzmetal and his associates[19] described a 53-year-old woman with hypertension resulting from bilateral renal infarction. Ben-Asher[20] reported the case of a 43-year-old white woman with renal infarction and hypertension who recovered and whose blood pressure returned to normal. Fishberg[21] reported four cases in adults in which an embolism of one or both renal arteries was followed by a rise in arterial tension.

Weber and his co-workers[22] recorded ten cases of thrombosis of the inferior vena cava in adults varying in age from 28 to 62 years. These cases were associated with pelvic sepsis (streptococcal septicemia), thrombophlebitis, trauma, aneurysm at the bifurcation of the aorta, carcinoma of the right testis, which was secondary to carcinoma of the kidneys and suprarenal glands, and massive carcinoma of the liver, probably arising in the bile ducts. Derow and his associates[23] described a case of chronic progressive occlusion of the inferior vena cava and the renal and portal veins in a 15-year-old boy who lived one year after the onset of thrombosis. Terminally, edema developed in the legs, scrotum and abdominal wall, with a suggestion of ascites. At post-mortem examination practically the entire inferior vena cava was completely occluded and replaced by a solid cord. The occlusion began at the junction of the common iliac veins. Lutembacher[24] reported a case of slow obliteration of the inferior vena cava which was compatible with life because of the anastomosis between this vein, the superior vena cava, and the portal vein. The collateral circulation assured sufficient function of the hepatic and renal parenchyma so that the patient was able to live fifteen years with complete obliteration of the inferior vena cava as well as the trunk of the portal vein and its two main branches. Thrombosis had occurred when the patient was 16 years of age.

The correct diagnosis is seldom made in these cases except at operation or by pathologic examination at necrospy. In the cases recorded in the earlier literature the diagnosis was made chiefly at post-mortem examination. Abeshouse,[12] in a review of 228 cases, noted that the diagnosis was made at post-mortem examination in 209 cases, at operation in fifteen cases, and clinically in four cases. The most important and valuable diagnostic procedure today is the excretory and retrograde urographic study. In 1942, Campbell and Matthews[17] were credited with having made the first correct preoperative diagnosis by retrograde pyelography as early as eighteen hours after the onset of thrombosis.

CASE REPORT

Clinical History.—A 4-month-old Negro boy was admitted to Children's

Hospital on Oct. 1, 1949. He was one of twins born prematurely in a neighboring hospital. Delivery had been normal. The other twin, who weighed 1 pound, 5 ounces, died at birth. Postmortem examination revealed bilateral fetal atelectasis, prematurity, and immaturity. The patient discussed here weighed 2 pounds at birth, and remained at the hospital in which he was born until he attained a weight of 5 pounds. He did well on evaporated milk, oleum percomorphum and vegetables until four days prior to admission to the Children's Hospital, when he started vomiting and having moderately severe diarrhea.

On admission, the infant appeared fairly well developed and well nourished, but slightly dehydrated. He had distinct pallor of the skin. A hemogram on admission showed 3,500,000 erythroctyes, and the platelets were within normal limits. Urinalysis on October 3 revealed the urine to be slightly cloudy and acid. The specific gravity was 1.010. The urine contained 10 mg. of albumin per 100 ml., 70 to 75 leucocytes in each high power microscopic field, many clumps, and few bacteria.

The patient was given fluids and a transfusion of 100 c.c. of whole blood. The following day he had six loose stools and appeared even more anemic than on admission. Fluids by hypodermoclysis with hyaluronidase (Alidase*) were given to correct the moderate dehydration. On the fourth hospital day, pallor was still present, scrotal edema developed, gross hematuria was noted, abdominal palpation revealed a large mass in each flank, and the child cried as though in severe pain. At this time, edema was observed also in the lower extremities. Total protein and the albumin-globulin ratio were normal, and the reticulocyte count was well within normal limits. A flat plate of the abdomen revealed hepatosplenomegaly. The large and small bowel was distended with gas and displaced toward the midline by bilateral flank masses. Roentgenologic examination revealed the long bones to be normal. The pallor persisted, and on October 5 a hemogram showed a fall in hemoglobin to 3.2 Gm. and a drop in erythrocytes to 1,000,000. On the sixth hospital day, the prothrombin time was 108 per cent of normal. Results of bone marrow studies were all within the range of normalcy. The patient was given another transfusion of 100 c.c. of whole blood because of the persistently severe anemia. Sickle-cell preparation revealed 25 per cent sickling, but on the following day another preparation was negative for sickling. A third transfusion of 100 c.c. of whole blood was given. Immediately thereafter, dyspnea and cyanosis developed, which necessitated oxygen therapy on October 6. Results of the Coombs' test, at this time, were negative. The child became oliguric and passed blood by rectum. The nonprotein nitrogen rose progressively from 42 mg. per 100 c.c. of blood on October 4 to 148 mg. on October 12. The systolic blood pressure was 102 mm. Hg, and the diastolic was difficult to detect between 50 and 60 mm. Hg. On October 13, the thirteenth day of hospitalization, the child was anuric. Intravenous administration of a 10 per cent solution of glucose was to no avail in inducing diuresis. The edema had progressed, with considerable edema of the extremities and some sacral edema. An intravenous pyelogram was contraindicated because of the anuria and the elevation of nonprotein nitrogen. A fragility test was performed and the results were within normal limits. Edema of the lower extremities and lumbosacral region progressed until death occurred on October 17, the seventeenth day of hospitalization, at which time the child was anuric and in uremia.

Post-mortem Examination.—Anatomical diagnoses were: bilateral hemorrhagic renal infarction, thrombosis of the renal veins and the inferior vena cava, pulmonary edema and emphysema, congestion of the ab-

*G. D. Searle & Co.

dominal viscera, thrombosis of the meningeal veins, and cerebral hemorrhage.

The post-mortem observations of special relevance will be described more fully.

Brain: The subarachnoid space contained an excessive amount of clear fluid. The vessels were congested. The rolandic veins on the right hemisphere were thrombosed to a point midway in the parietal lobe. The left rolandic veins were thrombosed to the sylvian fissure. There were several thrombosed veins which appeared to enter the longitudinal sinus. Coronal sections showed severe venous congestion. Within the right posterior parietal lobe was a hemorrhagic area measuring 7 × 3 × 3 mm. which was in the white matter of the brain and adjacent to the middle gyrus. A second hemorrhage was found in the right middle parietal lobe adjacent to the superior gyrus within the white matter.

Pituitary Gland: Microscopically, there was a predominence of eosinophilic cells in the anterior lobe of the pituitary gland. The posterior lobe revealed an infarcted area containing red blood cells in various stages of disintegration.

Lungs: Both lungs contained areas of increased density in both lower lobes. The surfaces were purple-gray and slightly depressed; they had the consistency of liver. Microscopically, the pleura was slightly thickened. There were scattered areas of atelectasis with some pink-staining homogeneous substances in the alveolar spaces, consistent with edema fluid.

Liver and Spleen: The liver edge extended 3 cm. below the right costal margin. The liver was firm, and on cut section revealed small yellow fatty areas. The spleen was somewhat flabby and on cut section was consistent with a splenic tumor. Microscopically, the liver showed hepatic edema, and the spleen showed congestion with distortion and compression of the germinal centers.

Adrenals: There were some deeply staining cells scattered throughout the cortex and some just beneath the capsule which resembled medullary cells. There were some red blood cells congested in areas of the medullary tissue.

Gastrointestinal Tract: A few polymorphonuclear cells were scattered throughout the submucosa of the intestine.

Inferior Vena Cava and Renal Veins: The entire inferior vena cava was distended and thrombosed distal to the liver as well as to the renal veins.

Ureters: The ureters were patent but thickened. They were blue, as if they had been stained with blood.

Kidneys: Both kidneys were enlarged to approximately four times their normal dimensions and were about equal to each other in size, measuring 5 × 8 cm. (Fig. 1). They weighed 100 grams each and had retained their fetal lobulations. They appeared hemorrhagic; their color varied from a deep red to a dark purple. In situ the organs lay 1 cm. apart in the midline (Fig. 2).

On section, the renal capsules were grossly thickened and stripped as if there had been a previous subcapsular inflammation. There was little if any difference between cortex and medulla, both of which appeared dark red as if severe passive congestion or hemorrhage, or both, had been present.

Microscopically, the cortex of the kidneys showed extensive leucocytic infiltration, with many polymorphonuclear leucocytes scattered throughout the area (Fig. 3). On the other hand, the medulla contained less leucocytic invasion but considerable necrosis, apparently on an ischemic basis. Cortical blood vessels were patent and allowed infiltration of leucocytes into the cortical tissue in contrast to the medulla which showed severe necrosis resulting from thrombosis. There was great destruction of the glomeruli and the tubules, with only an occasional glomerulus having retained its structure. Diapedesis of red blood cells in various stages of disintegration, amounting practically to hemorrhage in most areas, was seen. Within the medulla, small, scattered accumulations of hemosiderin were seen through-

Fig. 1.—Gross section of kidney which measured 5 × 8 cm. and weighed 100 grams. Note severe congestion.

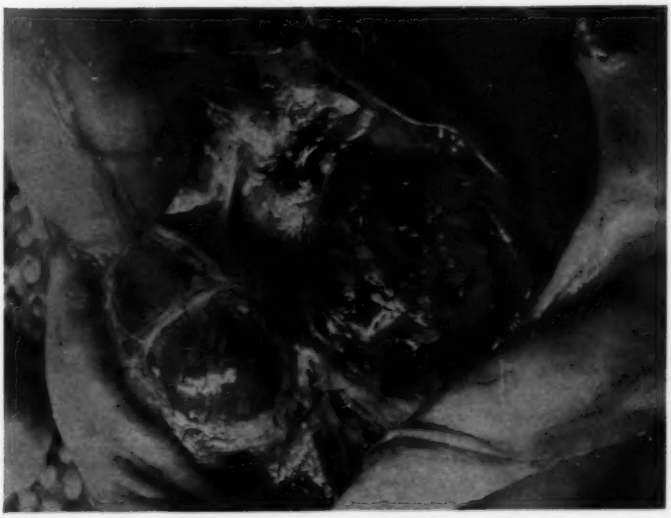

Fig. 2.—Position of the kidneys in situ. Note size and proximity to one another.

Fg. 3.—Microscopic section of kidney (low-power view) showing line of demarcation between cortex and medulla, with extensive leucocytic infiltration into the former.

out the necrotic tissue. There was loss of cytologic detail except for faint tubular outlines. Many of these faintly outlined tubules were considerably dilated. Polymorphonuclear cells had infiltrated the lumens of the thrombosed vessels as well as some of the renal parenchyma which was not completely necrotic. The extent of the necrosis varied from one area to another but appeared to be greater in the region close to the pelvis.

SUMMARY

A review of the literature on renal vein thrombosis and infarction of the kidneys revealed that this condition usually is a complication of diarrhea in newborn infants, that it is extremely rare, and that its exact etiology is unknown. In the case which has been reported, post-mortem examination showed massive thrombosis, including the inferior vena cava, rolandic veins, and renal veins, with bilateral hemorrhagic renal infarction (Fig. 2). Hypertension in these cases is exceedingly rare, but in this case the blood pressure appeared to be elevated.

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TREATMENT WITH AUREOMYCIN OF LOCALIZED PASTEURELLA MULTOCIDA INFECTION

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PASTEURELLA multocida infections of man are relatively rare. In a survey of the world literature from 1930 to 1947, Schipper[1] collected but twenty-one authentic reports on thirty-nine cases. These infections included pneumonia, pleurisy, septicemia, meningitis, appendicular abscess, and inflammatory lesions of the extremities. Four of the patients died. Indubitably, the cause of such infectious maladies may not be elucidated unless careful bacteriological studies are carried out. That *Past. multocida* infections may be more common than is appreciated at the present time is evident from the observation of Needham[2] to the effect that this organism could be isolated from eleven patients seen at the Mayo Clinic during the year 1947 and has since been isolated from a total of twenty-five patients.[3] Recently, we had the opportunity to observe a localized infection due to *Past. multocida*. Since the effectiveness of several new antibioties (aureomycin, terramycin, and bacitracin) upon this species had not yet been investigated, a study on the comparative efficacy of seven antibioties upon eight strains of *Past. multocida*, including the one isolated from our patient, was carried out. It was found[4] that this microorganism was highly sensitive in vitro to aureomycin, terramycin, Chloromycetin, polymyxin B, and penicillin, less so to streptomycin, and insusceptible to bacitracin. Since aureomycin was highly effective even in small amounts (0.1 to 1 μg per milliliter) against small and large numbers of *Past. multocida*, it was decided to investigate its clinical usefulness. The following report, then, describes the results obtained with this antibiotic in the treatment of a localized *Past. multocida* infection, and represents the first communication on aureomycin treatment of a human infection due to this microorganism.

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CASE REPORT

A. P. (No. 60191), a 15½-year-old white male, was injured on Sept. 17, 1944, "by a kick in the face by a horse." On the same day he was admitted to the Children's Hospital, and the diagnosis of compounded nasal fracture with nearly total loss of nasal bones and septum was made. A plastic repair was carried out. On June 21, 1949, a preserved human cartilage was implanted. Subsequently, purulent discharge from the region of the bridge of the nose developed. Since the inflammation did not subside, the discharge was examined bacteriologically on July 5, 1949. Many pus cells and scattered gram-negative bacilli were seen. The microorganism was identified as *Past. multocida*. The subculture of the strain was sent to the Communicable Disease Center and a report of *Past. multocida* was received from Dr. Frobisher. No other bacteria were present. The same microorganism was recovered subsequently on July 8 and July 16, 1949, and during a third admission to the hospital on April 28 and 29, 1950. It is reasonable to assume, then, that this localized infection was caused by *Past. multocida* and originated from the horse. *Past. multocida* is a well-known pathogen of animals. Whether the organism had remained dormant in the tissues since the original accident, and the infection was activated by the operation, cannot be stated with certainty.

Treatment with aureomycin was commenced on April 27, 1950. The anti-

biotic was given by mouth (500 mg. six times a day) and in the form of an ointment applied to the wound for three weeks. Within a few days after initiation of this therapy the discharge decreased considerably, and from May 4 on, *Past. multocida* could no longer be isolated. The patient was again seen on May 31, and the marked improvement has persisted even after discontinuation of specific therapy. However, on July 28, cellulitis developed and the patient was hospitalized on the following day. Cultural examination of the discharge revealed the presence of numerous group A hemolytic streptococci and coagulase-positive, hemolytic staphylococci of the aureus type, as well as rare *Past. multocida*. In vitro tests revealed that the strain was as susceptible to aureomycin as the original strain. Penicillin therapy resulted in immediate and satisfactory improvement, which has continued to date. All three organisms promptly disappeared. It is conceivable that *Past. multocida* had remained in the tissues without producing any noticeable damage and had become demonstrable during the attack of cellulitis, which undoubtedly was of streptococcal and staphylococcal origin. On August 2, the necrotic tissue, located just below the athenoids, was removed and the wall curetted down to healthy solid bone. Uneventful recovery took place and the patient has remained well to date. The culture of the material revealed the presence of *Staphylococcus aureus* (coagulase-positive) and *Pseudomonas aeruginosa; Past. multocida* was not present.

That aureomycin was effective in the treatment of this patient is evident from the facts that the purulent infection was present for ten months, that *Past. multocida* was demonstrable without difficulty during this period, and that marked clinical improvement took place within a few days after administration of this antibiotic was commenced. However, it is also clear from the data presented that the microorganism was not eliminated, but had persisted in the tissues without causing noticeable clinical injury, unless one postulates a second infection from without. The data obtained on the effects of aureomycin on growth of *Past. multocida* in vitro and in experimental *Past. multocida* infection of mice,[5] as well as the above clinical observation in a chronic localized infection, seem to justify further clinical trials with this antibiotic in *Past. multocida* infection.

SUMMARY

A chronic, localized infection of the nose due to *Past. multocida* and originating in all likelihood from a horse was treated with aureomycin given locally and perorally. The clinical response was favorable and the organism disappeared. However, it could be demonstrated again during the subsequent attack of cellulitis caused by hemolytic streptococcus and *Staph. aureus*, which was treated successfully with penicillin. The necrotic tissue was removed. The clinical and bacteriological improvement following cessation of all therapy has continued. In vitro, this strain proved to be highly susceptible to aureomycin and did not develop resistance to this antibiotic.

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SALMONELLA TYPHIMURIUM OSTEOMYELITIS

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OSTEOMYELITIS caused by Salmonella organisms is rarely encountered. Several cases of paratyphoid B osteomyelitis and a few due to other types of the Salmonella group[1-11] have been reported. Salmonella typhimurium has been found as the causative organism in four previous reports.[4, 5, 7, 9] However, involvement of multiple sites with this specific organism has been reported in only one case.[9] In that case there was involvement of all the ribs, the right scapula, the wings of the ilia, the neck of the left femur, and part of the right ileum near the acetabulum.

The following report is the second case involving multiple sites; namely, the right and left fourth metacarpals, right first and second and left fourth metatarsals, the right and left cuboids, the right astragalus, right fibula, right proximal first metatarsal, and the right first and third cuneiforms.

CASE REPORT

History.—J. V., a 14-month-old Negro female, entered The Children's Memorial Hospital on Nov. 16, 1949, because of irritability and anorexia for two weeks, elevated temperature for six days, and a swollen, painful right foot and ankle for five days. There were no gastrointestinal or urinary symptoms.

The birth and family histories were noncontributory. The past history revealed that she was hospitalized at another institution for "pneumonia" at the age of 5 months. At that time she developed diarrhea which persisted for a period of one month. From then until the age of 10 months she remained well when she was again hospitalized at the same institution for high fever and swelling of the hands and feet. After treatment for fourteen days with "penicillin and sulfa" she was discharged, apparently cured. She remained well until the onset of the present illness.

Physical examination revealed a toxic, lethargic, fairly well-nourished and well-developed Negro female child. There was a grade 3 systolic murmur heard over the entire precordium, maximum at the third to fourth left interspaces. The liver was palpable 5 cm. below the right costal margin, and the spleen was palpable below the left costal margin. There was also minimal nuchal rigidity but no Kernig or Brudzinski signs.

The right lower extremity was very hot with moderate swelling of the ankle and the entire foot. There was limitation of motion of the ankle. The foot was puffy and tender. The range of motion from the knees and hips was normal. There was no fluctuation. Subcutaneous nodules were not felt. The reflexes were normal bilaterally. Examination of the right hand showed a tender subcutaneous nodule on the dorsum, situated between the third and fourth metacarpals. There was a slight swelling of the hands.

Clinical Course.—For ten days (Nov. 16 to 25, 1949) the patient ran a septic temperature, the fever ranging from 101 to 105.2° F. From that time until discharge she was afebrile. The blood showed profound anemia plus 100 per cent sickling of the red blood cells. Blood transfusions were given on December 18 and 22, and iron and vitamins were administered orally.

Early in the course of her illness she was very irritable and ate poorly. On

From The Children's Memorial Hospital and the Ortho S.A. Sprague Memorial Institute Laboratories.

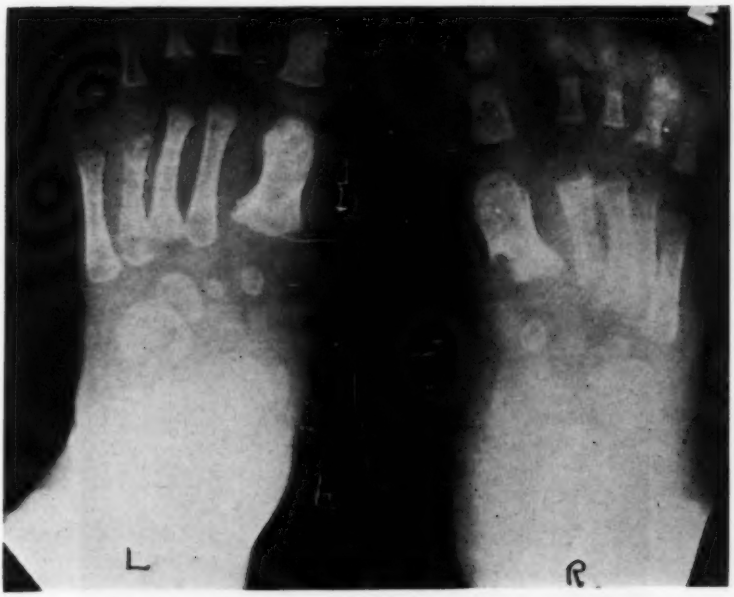

Fig. 1.

Fig. 2.

November 21, a purulent material began to drain spontaneously from the dorsum of the right foot. The entire right lower extremity to the knee was swollen and tense, as were the right hand and left foot. There was also marked tenderness over these areas. Roentgenographic examinations revealed "marked bone destruction involving the right fourth metacarpal with evidence of periosteal new bone formation. Similar such destruction, but not to as great a degree, is present in the right second metatarsal and the left fourth metatarsal. There is also an irregular area of destruction of the proximal cuboid" (Figs. 1 and 2). On December 8, there was radiological evidence of involvement of the right fibula, left fourth metacarpal, right first metatarsal, right first and third cuneiforms, left cuboid, and right astragalus. Complete x-ray studies of the remainder of the skeletal system, including the skull, spine, ribs and pelvis, were negative.

Fig. 3.

Hot, moist dressings were started on November 22, after aspiration of the abscess of the right hand. There was little improvement, and on November 25, incision and drainage of the fluctuant areas over the right lateral malleolus and dorsum of the right hand were performed. A large quantity of creamy pus was evacuated and cultured.

Penicillin G, 50,000 units every three hours, was started at the time of admission. Duozine Liquid,* 0.3 Gm. every six hours, and streptomycin, 125,000 units every six hours, were started on November 21. Aureomycin, 50 mg. every four hours for five doses daily, was started on November 22, when a smear of the pus from the right foot revealed "gram-negative bacilli."

three hours, which was continued until December 22.

The patient slowly improved, and on December 15 there was only a slight swelling and tenderness of all the involved sites, and all the purulent drainage had ceased. The patient was discharged on Jan. 18, 1950.

Follow-up roentgenographic studies revealed the following: Jan. 10, 1950:

Fig. 4.

The causative organism, *S. typhimurium*, was found on November 28, and all medication was discontinued in favor of Chloromycetin, 125 mg. every

"After therapy the lesion in the shaft is thicker and slightly denser than the surrounding bone, but generally it has been entirely reconstituted. Lateral views of the right lower tibia and ankle reveal extensive destructive changes in the distal two-thirds of the astragalus and minimal periosteal elevation of the

*This drug was supplied to us by the Abbott Laboratories, North Chicago, Ill. It is their registered trademark for suspension of sulfadiazine, 0.15 Gm., and sulfamerazine, 0.15 Gm., with 1.5 Gm. sodium citrate in 5 c.c. of a flavored suspension base.

LABORATORY DATA

Blood Counts

DATE	HB	RBC	WBC	P	L	M	E	B
11-17-49	6.5	2.77	26,300	70	29	1	0	0*
11-28-49	7.5	3.86						
12- 6-49	6.5	2.47	13,300	22	73	4	0	0
12-14-49			15,500	25	67	7	1	0
12-27-49	9.3	4.14	13,300	17	80	3	0	0
1-27-50	8.3	2.78	24,000	24	66	3	3	1
2-30-50	6.9	2.53	29,700	43	49	5	3	0
3-30-50	7.4	2.93	14,100	63	26	7	1	0
4- 3-50	11.5	3.96	15,900					
5-12-50	8.5	3.63	18,300	18	79	0	3	0

*100 per cent sickling in four hours. Moderate macrocytosis and poikylocytosis. Marked hypochromia.

Mother's blood revealed sickling of 25 to 50 per cent in twenty-four hours on Feb. 23, 1950.

Blood Chemistry: Calcium, phosphorus, and alkaline phosphatase determinations on repeated occasions were within normal limits.

Urine: Repeated urinalyses were negative for sugar, albumin, and cellular elements.
Culture (Nov. 26, 1949) revealed *S. typhimurium*.
Cultures (Dec. 9, 1949, and Jan. 6, 1950) were negative.

Blood Cultures: (Nov. 17, Nov. 18, Dec. 17, 1949, and Jan. 6, 1950) were negative.

Stool Specimens: (Nov. 25, 26, 28, Dec. 1, 1949, Jan. 5, 7, 1950) for parasites and ova and culture were negative.

Lumbar Puncture: (Nov. 16, 1949) revealed no cells. Negative Pandy. Protein, 11.3 mg. per cent; sugar, 99 mg. per cent; and chlorides, 648 mg. per cent. There was no growth on culture.

Mantoux: (Nov. 18, 1949) 1:1,000, Negative.

Kahn and Wassermann: (Nov. 18, 1949) Negative.

Cultures From Purulent Material:
Right Hand:
(Nov. 21, 1949) Positive for *S. typhimurium* (State Health Laboratory).
(Nov. 28, 1949) Positive for *S. typhimurium* (State Health Laboratory).
(Dec. 2, 1949) Negative.
Right Foot:
(Nov. 21, 1949) Positive for *S. typhimurium* (State Health Laboratory).
(Dec. 2, 1949) Negative.
(Dec. 12, 1949) Negative.
Left foot:
(Nov. 21, 1949) Positive for *S. typhimurium* (State Health Laboratory).
(Dec. 2, 1949) Negative.

Agglutinations

					STOCK		PATIENT'S ORGANISM	
DATE	TYPH O	TYPH H	PARA A	PARA B	ST* O	H	ST O	H
Nov. 17, 1949 CMH†	neg.	neg.	neg.	neg.				
Dec. 1, 1949 SHL‡	neg.	neg.	neg.	1:80§	neg.	neg.		
Dec. 17, 1949 SHL	1:80§	neg.	neg.	1:320	neg.	1:2,560		
Dec. 29, 1949 SHL	neg.	neg.	neg.	1:320	1:320	1:1,280	1:320‖	1:5,120
Jan. 27, 1950 SHL							1:320	1:2,560
Feb. 23, 1950 SHL							1:40	1:640
Apr. 20, 1950 SHL							1:160	1:320
Jun. 15, 1950 SHL							1:160	1:80

*S. typhimurium.
†The Children's Memorial Hospital Laboratory.
‡State Health Laboratory.
§Borderline dilution. Higher dilutions are considered positive.
‖From this date on, patient's own organism and serum were used.

lower fibula. There is marked regeneration of the right fourth metacarpal." (Figs. 3 and 4.) April 20, 1950: "There has been complete regeneration of the metatarsal lesions. The cuboid lesions remain essentially unchanged as well as the lesion in the astragalus. There has also been complete recovery in the fibula." (Fig. 5.)

She was readmitted March 30, 1950, for a blood transfusion because of her sickle-cell anemia and was discharged April 4.

COMMENT

S. typhimurium osteomyelitis involving multiple sites is rarely encountered, this being the second case to be reported in the literature. It is probable that this infection may have started at the time of the patient's second hospitalization at 10 months of age when she had a swelling of the extremities. A more severe exacerbation occurred four months later when she was hospitalized at The Children's Memorial Hospital.

Fig. 5.

When seen in the Outpatient Department on Jan. 28, 1950, the patient was entirely asymptomatic and standing with support. However, some swelling and tenderness of the dorsum of the right foot still persisted. She was examined again on April 20, at which time there was still slight swelling of the right foot but no tenderness. The patient was now able to walk with support. When last seen on June 15, the findings were the same except that the patient was able to walk alone and had been doing so for approximately five weeks.

Clinically, she improved on sulfadiazine, penicillin, and aureomycin. There was no toxicity, and the patient was afebrile when cultures of the purulent material revealed *S. typhimurium*. At this time she was treated with Chloromycetin alone. After eight days' treatment with Chloromycetin, the cultures

became negative. Never to our knowledge has a patient with Salmonella osteomyelitis been treated with Chloromycetin and with complete recovery. A case of *Eberthella typhosa* osteomyelitis successfully treated with Chloromycetin was reported by Morse and Geiser.[12]

The etiological organism was firmly established by positive cultures from multiple abscesses and from the urine. The agglutination titer with the specific organism and the patient's serum rose to a height of 1:5,120. These bacteriological and serological determinations were performed by the Illinois State Health Laboratory.

Convalescence was protracted, but after an eight-month follow-up there appears to be complete recovery.

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Medical Progress

A REVIEW OF THE SURGICAL TREATMENT OF INTERNAL HYDROCEPHALUS

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IN SPITE of the tremendous advances that have been made in the field of neurological surgery, the treatment of hydrocephalus has remained for many a discouraging problem. The recent impetus on the surgical treatment of hydrocephalus has prompted this review. From the latter part of the nineteenth century up until World War I, there were occasional reports on various treatments of hydrocephalus, some of which met with success. The number of cases was small, and the follow-ups were not sufficiently long to warrant universal practice. About twenty years elapsed before other procedures were undertaken for the treatment of this condition.

Internal hydrocephalus is either communicating or noncommunicating (obstructive). Noncommunicating internal hydrocephalus occurs when the cerebrospinal fluid is obstructed at any point between its formation in the lateral ventricles and its exit from the fourth ventricle. Communicating internal hydrocephalus, on the other hand, describes a condition where the fluid is obstructed beyond the fourth ventricle.

PATHOLOGICAL PHYSIOLOGY OF INTERNAL HYDROCEPHALUS

Before considering the various treatments of hydrocephalus, certain anatomical, physiological, and pathological facts must be accepted. It seems well established that the cerebrospinal fluid is formed by the choroid plexus. However, the exact role the choroid plexus plays has not been determined. At present two main theories exist: (1) that the choroid plexus acts as a secretory body,[1] and (2) that it acts as a filter.[2] More important to our present subject matter is the absorption of cerebrospinal fluid. The bulk of evidence at hand favors absorption of this fluid directly into the blood by the arachnoid villi from every part of the subarachnoid space.[1]

Internal hydrocephalus is thought to be caused by (1) overproduction of cerebrospinal fluid, (2) blocking of arachnoid villi with decreased absorption of cerebrospinal fluid, or (3) by an obstruction of the flow of cerebrospinal fluid through the ventricular system.

Overproduction of cerebrospinal fluid from the choroid plexus has been considered to be due either to a diffuse hypertrophy of the choroid plexuses or to a thrombosis of the great vein of Galen. Dorothy Russell[3] in her classical monograph on pathology of hydrocephalus pleads for reservation in acceptance that hydrocephalus occurs as a result of hypertrophy of the choroid plexus. She refers to a case of her own, where, on gross inspection,

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one would accept hypertrophy of the choroid plexus as the etiology of the internal hydrocephalus, but on further microscopic examination a chronic low-grade meningitis was observed, causing obliteration of the absorbing surface. Dandy and Blackfan[4] were the most prominent proponents of hydrocephalus following thrombosis of the great vein of Galen. They occluded the vein of Galen in ten dogs, and only one developed hydrocephalus. Bedford[5] ligated this vein in forty-seven dogs and in none of the animals did hydrocephalus develop. Schlesinger[6] confirmed Bedford's findings in the monkey. It is truly amazing that such a false concept arose from a single animal experiment.

Alteration of the arachnoid villi by disease results in damming back of spinal fluid and, ultimately, some degree of hydrocephalus. The block may be due to adhesions as result of inflammation or trauma directly obliterating the absorbing area, thrombosis of the dural sinus obliterating the villi which absorb the cerebrospinal fluid, or compression of the subarachnoid space and villi in increased intracranial pressure resulting from expanding lesions as neoplasms, hematomas, or abscesses.

Obstruction in the cerebrospinal fluid pathways is responsible for at least 99 per cent of cases of internal hydrocephalus.[3] In each of Dorothy Russell's pathological specimens of internal hydrocephalus some block of the cerebrospinal fluid pathways was observed.

SURGICAL TREATMENT OF INTERNAL HYDROCEPHALUS

Accepting these theories for the pathogenesis of internal hydrocephalus, it would seem that any surgical therapy should aim at by-passing the obstruction and allow for absorption of cerebrospinal fluid. Many ingenious methods have been devised to accomplish this, but not until recently have any been satisfactory.

Of the present-day treatments, there is hardly one that had not been carried out around 1900. The type of surgical treatment depends on whether the hydrocephalus is communicating or noncommunicating. In communicating hydrocephalus, the avenues are open for either a reduction in production of fluid or an enlargement of the reabsorbing area. These principles have led neurosurgeons to remove partially or totally the choroid plexus, or shunt the cerebrospinal fluid to other spaces, cavities, or the vascular system. In noncommunicating hydrocephalus, the main principle has been to avoid the obstruction at the aqueduct.

Of those procedures concerned with diminishing the amount of cerebrospinal fluid by attacking the source of fluid, carotid ligation by Stiles,[7] in 1898, was perhaps the earliest. He felt that cerebrospinal fluid was most likely produced from the choroid plexus, and attempted to diminish its blood supply. Fraser and Dott[8] and others carried out this procedure but abandoned it as useless. Deep x-ray therapy to the choroid plexus has been suggested to cause a diminution of fluid production.[9, 10] As early as 1904, Hildebrand[11] extirpated the choroid plexus. It was Dandy[12] who popularized the procedure. Coagulation of the choroid plexus was first attempted by Lespinasse[13] as early as 1910. Putnam[14, 15] and others have improved on

this method and have had successful results with selected cases. It is estimated that perhaps 50 per cent of patients so treated are benefited. Hyndman[16] in removing the choroid plexus disrupted the laminae of the choroid plexus and established a communication from the lateral ventricle through the tela choroidea to the cisterna venae magna, cisterna ambiens, and to the cerebral subarachnoid space. He felt that the good results obtained from cauterization of the choroid plexus "may be due partly, if not chiefly, to the unwitting creation of such a fistula through the choroidal fissure rather than to a diminished production of ventricular fluid." Royle,[17] in 1938, felt that a cervical sympathectomy would increase the absorption of cerebrospinal fluid. This does not seem like a very logical procedure and only one case has been done.

Among the oldest operations known for the treatment of hydrocephalus is puncturing the lateral ventricles and removing the fluid. Hippocrates is reported to have done this.[18] Quincke[19] introduced the method of lumbar puncture and drainage of the lumbar spinal fluid in the treatment of hydrocephalus. This method seemed to help some patients with hydrocephalus by allowing a balance between absorption and formation to take place. Removal of cerebrospinal fluid by either of the two methods described is, at best, a temporary procedure.

In 1884, Pollock[20] attempted to drain cerebrospinal fluid to the surface of the head. Other surgeons during that period carried out the procedure, but varied the technique somewhat. Horsehair, glass tubes, silver thread, catgut, rubber and gold cannulae were some of the items used to establish drainage. McArthur passed a gold cannula from the ventricle to beneath the scalp.[21] Watson, Cheyne, Ballance, Andrews, and others connected the lateral ventricle to either subarachnoid or subdural space with a gold or platinum tube.[21] This procedure was only temporary as either the drain became occluded or infection set in. Alfred Parkin[22] inserted a horsehair drain over the cerebellum and drained fluid to the tissues just beneath the skin in the neck region. After a number of unsuccessful attempts by others, this procedure was abandoned. Gartner suggested the establishment of a communication between the cerebrospinal fluid and the venous system and this was first put into practice by Payr,[23] in 1908, using a transplanted saphenous vein to join the lateral ventricle with the superior longitudinal sinus. Cushing[24] inserted a silver tube into a dilated third ventricle and passed it up through the corpus callosum into the longitudinal sinus. There have since been variations of this procedure of shunting the ventricular fluid to the venous system. Cone[25] had shunted the ventricular fluid to jugular vein or sagittal sinus by means of a plastic tube. His results were not encouraging. Recent experimental work of Ingraham and collaborators[26] shows that the ventriculovenostomy will work only while the intracranial pressure is high. As soon as the intracranial pressure approaches normal, the vein will thrombose. This convincing experimental work should cause abandonment once and for all of this procedure.

In 1893, Miekulicz[18] removed a large piece of cerebral hemisphere in an attempt to connect the ventricle with the subarachnoid space. This was unsuccessful because adhesions soon developed around the operative defect obliterating the surrounding subarachnoid space. Others attempted to open into the corpus callosum, but this, too, was abandoned as the vents closed.

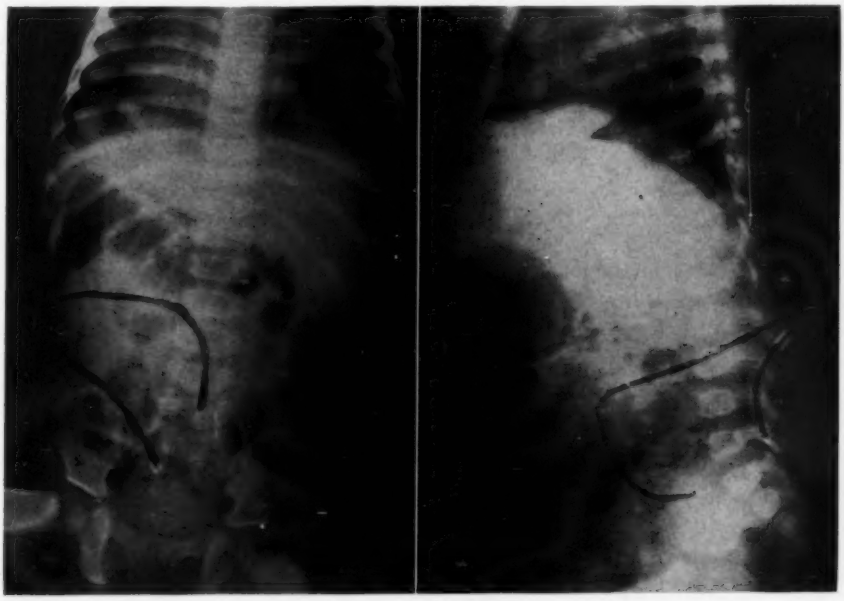
The presence of a large absorbing area as the peritoneal cavity was thought by some early surgeons to be a good site for the absorption of excess cerebrospinal fluid. In 1905, Kausch[18] united the lateral ventricle with the peritoneal cavity by means of a small rubber tube. The patient died seventeen hours later, and Kausch thought that the exodus was due to the rapid escape of cerebrospinal fluid from the ventricular system. Hartwell[18] carried out a similar procedure in 1910 using silver wire instead of a rubber tube. The child died two years later as a result of a tumor of the aqueduct of Sylvius without evidence of increased intracranial pressure. At autopsy there was present a tube of scar tissue surrounding the wire from the ventricle to the peritoneum. This scar tissue tube was patent and cerebrospinal fluid flowed freely. Ferguson[27] first reported draining spinal fluid from the lumbar subarachnoid space to the peritoneal cavity. In 1898, he reseeted the arch of the fifth lumbar vertebra, drilled a small hole through the body of L-5, and passed a loop of silver wire from the spinal subarachnoid space into the peritoneal cavity. His first patient died shortly after operation, and the reason was thought to be a sudden loss of fluid. His second patient improved as a result of the operation but expired three months later with bronchopneumonia. Cushing,[28] in 1908, added a laparotomy to the Ferguson technique. He reported considerable success in twelve patients but soon discarded the procedure because two or three patients had developed intussusception and died. He believed that the intussusception had been provoked by the presence of some substance, probably posterior lobe extract, which stimulated abnormal peristalsis. In some of his patients the drainage was actually retroperitoneal and not peritoneal. Cushing's procedure fell into disrepute before World War I and for the following thirty years all peritoneal shunts in the treatment of hydrocephalus had been virtually abandoned.

More recently, Cone, Lewis, and I[29] have reverted to the peritoneal shunts. We believed that the failure of peritoneal shunts was mechanical and not physiological. Most of our shunts were from the ventricle to the peritoneum. A plastic tube was placed into the ventricle and passed subcutaneously down to the peritoneal cavity. Some lumbar subarachnoid peritoneal shunts were carried out, but these were not successful and the procedure was discontinued temporarily. For the past several years only ventriculo-peritoneal shunts were carried out. This procedure has met with a moderate degree of success, but the follow-up has not been sufficiently long to warrant separate publication. In the early spring of 1950, I have again attempted in two patients the lumbar subarachnoid-peritoneal shunt with

success, but again the follow-up has been too short to advocate its general usage.

Heile (1927)[30] reported having kept a patient alive for eight years by shunting the fluid from the lateral ventricle to the pleural cavity. He secured patency of the tube by freeing adhesions at repeated operations. Because of the necessity for multiple operations this procedure had to be abandoned. Recently, Ingraham and associates[31] carried out shunts from the ventricle to the pleural cavity in animals with experimentally produced hydrocephalus. They concluded that the pleural space is capable of absorbing isotonic saline without losing its negative pressure, but that until further improvements in technique and materials were made, ventriculothoracostomy was not a promising procedure.

In 1925, Heile[32] published his findings on the drainage of cerebrospinal fluid into the urinary bladder. He removed one kidney and implanted the ureter intraspinally. He abandoned this procedure because of the high mortality rate. More recently, Matson[35] has carried out a similar procedure by removing a kidney and inserting a plastic tube from the lumbar subarachnoid space into the ureter. This has met with some popularity but, again, the follow-up has not been sufficiently long. Among his earlier cases some deaths occurred which subsequently were found to be due to excess sodium loss.[36] This has since been



A. *B.*

Fig. 1.—Photographs of x-rays showing position of plastic tube in lumbar subarachnoid peritoneal shunt. Tube has been retouched for photography. The tube is placed in the subarachnoid space at level of the fourth lumbar vertebrae. Patient L. A., aged 4 months, No. 4304-G, University of Texas. *A*, Anteroposterior view; *B*, lateral view.

remedied in the postoperative management. The main disadvantage of this procedure is the removal of one kidney. Another criticism is the insertion of an irritating substance as a plastic tube in the lumbar subarachnoid space. Cone and I have inserted such plastic tubes in the lumbar subarachnoid space in dogs and sacrificed the animal at varying periods. In all specimens there was present a marked proliferation of fibroblastic activity surrounding the tube and adjacent nerve roots. This makes one wonder what will happen to the nerve roots in these children after a prolonged period of time. This criticism is also applicable to the lumbar peritoneal shunt.

Nosik,[37] in 1950, introduced the ventriculomastoidostomy as the latest of shunting procedures. He inserted a plastic tube from the lateral ventricle to the antrum of the mastoid thereby draining cerebrospinal fluid into the nasopharynx. From 1947 to 1950 he had performed this operation on nine patients with communicating hydrocephalus with only one instance of postoperative meningitis. The objection to this procedure is the possibility of future meningitis from an ear or upper respiratory infection. This would seem to be a real possibility.

Noncommunicating hydrocephalus due to an obstruction in the third ventricle, the aqueduct of Sylvius, or the fourth ventricle is best treated by circumventing the fluid around the obstruction so that it may pass over the cerebral hemispheres and be absorbed. The procedure that has been most successful over a number of years in the hands of many different neurosurgeons is that of Torkildsen's ventriculocisternostomy. A catheter is inserted into the lateral ventricle through an occipital burr hole and then carried over the occipital bone to be placed in the cisterna magna.[38] Over the past five years, the literature contains numerous reports to attest for the success of this operation. Atresia or stenosis of the aqueduct of Sylvius also has been treated by catheterization of the aqueduct. Dandy[39] first carried out this procedure but later discarded it. Recently, Leksell[40] has catheterized the aqueduct and left a spiral metal cannula in place between the third and fourth ventricles. Surely, cannulization of the aqueduct is not the procedure of choice since we know the amount of damage done by a slight amount of trauma to the aqueduct. There are occasional reports of cannulization of the aqueduct as being successful, but on the whole, one would prefer a simple procedure as the Torkildsen operation, which is relatively atraumatic. Reichert[41] advocates passing a catheter from the lateral horn to the cerebellomedullary cistern through the tentorium for obstructive hydrocephalus. Since part of the cerebellum may have to be resected, it offers nothing over the ventriculocisternostomy and should not be advocated. Dandy[42] advocated making an opening in the floor of the third ventricle (either by the subfrontal or transtemporal approach) for obstructions in the aqueduct or fourth ventricle. This procedure, third ventriculostomy, has enjoyed some popularity but, on the whole, it has not been very successful. For the most part, the openings in the third ventricle have closed off. The indications for this procedure are rather limited.

It is applicable only when it can be proved that cerebral subarachnoid spaces are open. We certainly know that in the cases of long-standing hydrocephalus often the cerebral subarachnoid spaces become closed due merely to the prolonged increased intracranial pressure. Certainly, this is true in cerebral neoplasms when the pressure has been elevated over a long period of time and gradually occludes the cerebral subarachnoid spaces. This may also account for the failure of the Torkildsen procedure in addition to technical reasons. However, after the increased intracranial pressure has been relieved for several weeks or so, these cerebral subarachnoid spaces usually open in the case of a neoplasm.

SUMMARY

The procedures that are enjoying popularity today in the treatment of noncommunicating hydrocephalus are the ventriculocisternostomy of Torkildsen and the third ventriculostomy of Dandy. Torkildsen's procedure has met with the satisfaction of most surgeons. In selecting the third ventriculostomy, there is one essential prerequisite. It must be determined that the cerebral subarachnoid spaces are open before this procedure may be used.

In the case of communicating hydrocephalus, perhaps, the coagulation of the choroid plexus has been most universally used and has been successful in about 50 per cent of selected cases. However, many ingenious methods for shunting the excess cerebrospinal fluid from the ventricle and lumbar subarachnoid spaces have been devised and are replacing removal of the choroid plexus as the procedure of choice. The follow-up is still too short to determine which shunt will finally be the most successful. In evaluating the results, one must remember that a small percentage of patients undergo spontaneous recovery.

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Psychologic Aspects of Pediatrics

THE PREVENTION OF NEUROSES

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THE pediatrician and general practitioner are in key positions to advise parents and others, who care for young children, in general methods aimed at the prevention of neuroses and emotional disturbances.

Neuroses are distorted emotional processes, characterized by disguised expressions of accumulated guilt-tinged, hidden hostilities. The most important factor is an unhealthy way of handling natural emotions or of solving conflicting feelings or desires. Guilt feelings, anxiety, and hopelessness arise to cloud the issue. Under such conditions, even the natural physiologic reactions to real or apprehensive danger may be seized upon as signs of illness. Examples are heart pounding, painful stomach contractions, and paralyzing tingling throughout the body. Other complicating tension pains and obsessions, compulsions, and hysterical paralytic or amnesic symptoms may develop. The process is not adequately under the control of rational reasoning.

In reality, the process is less complicated than it seems, once we penetrate the usual smoke screen of confusing details. The study of the formative stages in young children gives clues to prevention.

There is a definite connection between neuroses and aggressive behavior problems. The connecting link is the way in which hostile feelings and resentments are either held in and their existence denied by repressive guilt, or the way they are allowed direct expression in aggressive behavior. When primitive rage reverts back into the source, tension and anxiety appear and neurotic fears may become manifest. This rage is intensified by frustration in the face of the youngster's usual omnipotent concept of his wishes. The neurotic misunderstands parental aims when the red glaze of anger distorts his concept of reality.

Hostility and repressive guilt are the common threads which are taken for granted and run through practically all schools of psychiatric practice and research findings. They need to be emphasized anew and are readily accessible points for the attack on prevention. The other varied inner complex factors in the production of neuroses are secondary in importance in that they are not so controllable. Also difficult to keep in bounds are first, parental deficiencies in giving the child the needed security or positive affectional experiences, and, second, some destructive social and cultural factors. What can be done about this guilt-tinged aggressive hostility, which is so productive of neuroticism?

Is it possible to teach suppressive control without repressive denial of hostile impulses? If so, a clue to the prevention of neuroses is the attainment of control without repression. Excessive punishment and shaming only serve to increase the causative submerged hostility and unnecessary

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Relationship of Neuroses to Aggressive Behavior **Chart I**

Experience	Age	Reaction
Breast fed		Quiet contented baby
Milk failed-Given bottle	1	Took bottle quietly
Weaned		No unusual reaction to weaning
Mother ill-Child put in nursery 6 weeks	2	Constant crying. Intense Tempers
Mother becomes pregnant, apprehensive and fussy	3	Prolonged crying. Temper tantrums. Breaks cup
Brother born-Child placed in neighbor's home 4 weeks		Cried constantly to return home Some food refusal, vomiting and occasional diarrhea
Baby brother absorbs Mother's attention	4	Fears of dark. Nightmares
Suppressive management by unhappy, resentful Mother		Complete personality change Mean - Unhappy
School Marks: Work / Conduct		Nightmares and Fears persist
1st Grade: D / B	5	
1st Gr. repeated: C / B	6	
2nd Grade: D / B	7	(Neurotic Symptoms Stop at 8)
2nd Gr. Repeated: C / C	8	Aggressive fighting behavior begins in school. Overactive.
3rd Grade: C / D	9	Seems mentally backward. Fights children. At home is better behaved and considerate. Occasionally jealous of brother. However, boy becomes grave problem to severe Woman teacher. Boy blurts out, "I don't worry none! I worry the kids and teacher."

Breast fed — Quiet contented baby
Milk failed-Given bottle — 1 — Took bottle quietly
Weaned — No unusual reaction to weaning
Mother ill-Child put in nursery 6 weeks — 2 — Constant crying. Intense Tempers
Mother becomes pregnant, apprehensive and fussy — 3 — Prolonged crying. Temper tantrums. Breaks cup
Brother born-Child placed in neighbor's home 4 weeks — Cried constantly to return home; Some food refusal, vomiting and occasional diarrhea
Baby brother absorbs Mother's attention — 4 — Fears of dark. Nightmares
Suppressive management by unhappy, resentful Mother — Complete personality change; Mean - Unhappy
Nightmares and Fears persist — 5
(Neurotic Symptoms Stop at 8) — 8
Aggressive fighting behavior begins in school. Overactive. Seems mentally backward. Fights children. At home is better behaved and considerate. Occasionally jealous of brother. However, boy becomes grave problem to severe Woman teacher. Boy blurts out, "I don't worry none! I worry the kids and teacher." — 9

School Marks	Work	Conduct	Age
1st Grade	D	B	5
1st Gr. repeated	C	B	6
2nd Grade	D	B	7
2nd Gr. Repeated	C	C	8
3rd Grade	C	D	9

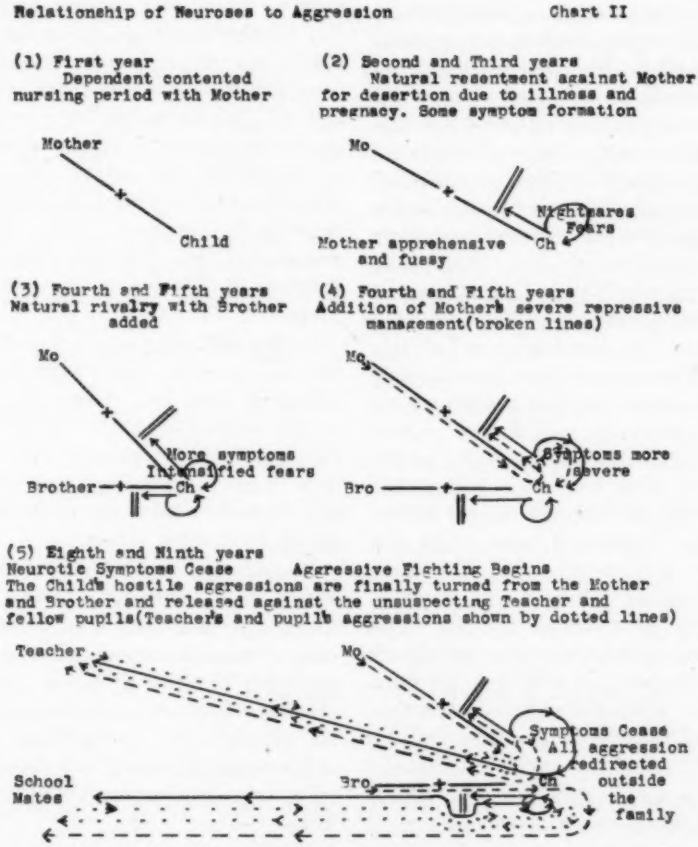
guilt feelings. It is well known that releasing and minimizing the inner tensions are a necessary part of sound recovery.

Simple diagrammatic case examples, occurring in young children, show the disappearance of the fear symptoms after drawing out aggressive behavior and discharging the repressed hostilities in action.

The relationship between neurotic symptoms and aggressive behavior is not always clear, but is strikingly shown by Charts I and II with the story of one boy's childhood.

As a baby, this youngster was quiet and contented until, in his second year, he was put in a nursery for six weeks while his mother was ill. There, in strange surroundings, he cried and had tempers. The next year, his mother was upset by an unexpected pregnancy and became apprehensive and fussy. The youngster's reaction to this was more crying and temper tantrums. When his brother was born, he was placed in a neighbor's home for a month. While again away from his mother he was extremely unhappy, and he would frequently not eat and had stomach upsets. In his fourth year, he developed unhappiness, fears, nightmares, and annoying behavior. This occurred when his burdened mother be-

came irritated, impatient, and severe. She was absorbed in the care of the new baby and unequal to also caring for her home, domestic troubles, and two small children. She was particularly exasperated at this older son's bed-wetting. The first three years at school he was poor in his lessons, but quiet and fairly well behaved in school. However, at home he remained "nervous," difficult, and still subject to fears and nightmares. At the age of 8 years, the additional disappointments, such as having to repeat the second grade and encountering a severe teacher, led to open rebellion and the release of his aggressions toward his school contacts. Then, the symptoms of the neuroses, the fears, nightmares, and even the bed-wetting rather abruptly disappeared. This boy's fundamental problems remained, but his manner of handling them had changed. The lad expressed this by blurting out, "I don't worry none, I worry the kids and the teacher."



The child's experiences are listed in Chart I on the left and his behavior reactions on the right, with the central column representing the various ages

at which they occurred. Neurotic symptoms appeared when hostile resentments were held in and submerged from consciousness. They disappeared spontaneously at 8 years of age, when the aggression was directed outwardly. Fighting and annoying problem behavior signified the failure of repression and emergence of these same hostile emotions.

The earlier repressive, shaming management of the unhappy, resentful mother led first to the accentuation of fears, disturbing dreams, and personality change. The repetition of the second grade at 8 years of age and other accompanying resentment-inducing incidents apparently overcame the repressive guilt feelings and allowed the emergence of accumulated hostile rage, which so colored the youngster's actions to his schoolmates. Meanwhile, also in his eighth year, he was lectured more and his fighting was forbidden at home. At the beginning of this fourth school year, a new second grade woman teacher applied a rigid regime in the schoolroom, and the boy reacted explosively. No doubt loyalty to his mother, which had been drilled into him by the family, also caused his behavior to improve at home. The new teacher unwittingly used the same severe tactics, but was not protected by the adopted family loyalties. This boy thus also became very troublesome in the classroom as well as on the playground. When his withholding repression was relieved in this direction, his neurotic symptoms completely ceased.

The accompanying diagrams (Chart II) depict the currents of feeling flowing between this boy and others with whom he came in contact. The first four diagrams illustrate the way in which such emotions are handled under repressive influences and accompanying guilt feelings. The positive ties are marked with a plus sign. The currents of aggression are plain and broken lines, with the source and direction indicated by an arrow. The forces of conscience or guilt are represented by the perpendicular parallel lines deflecting and turning back the course of hostile emotion. When primitive antagonistic feelings revert back into the source, tension and anxiety appear and neurotic fears may become manifest. The broken lines from the mother represent her severe, resentful management which engendered more hostility and also reinforced the barriers blocking the expression of the boy's feelings to herself and his brother. The stage was set for the evaporation of the neurosis by the explosive action against schoolmates and the rigid repressive teacher, as depicted in the fifth diagram.

In the following example, a 6-year-old boy lost his fears after he was helped to face and release his guilt-tinged submerged angry resentments. He had attributed his own hostile feelings to his surroundings and personified them as an imaginary Witch, of which he became afraid.

Donald was the older of two children. He was slow in his second grade schoolwork, and tattled on other children. Investigation revealed childish annoying behavior at home. He was fearful, self-conscious, disrespectful to his grandmother, disobedient, jealous of his younger brother, and destructive with toys. Punishment only made him worse.

When examined, Donald was found to be intelligent and physically healthy.

During the treatment, the boy himself confided to the psychiatrist that

he had "lots of dreams" and was afraid of the dark. "I dreamed a Witch was under my bed and she killed me by sticking her nose in me." He drew a face with a long pointed nose. "I am afraid to go to bed because—because I dream and think it is true." He had had this fear "for a long time."

When asked who the Witch reminded him of, he hesitated and said, "My grandmother."

He was afraid, "Because I think there are things in the dark."

"What?"

"The Witch."

"My house is an old one and a wall might fall down, It scares me when the water runs. Last winter when I had my nap, the sink got filled up and spilled over. I heard the noise and went in there and called my mama."

"No, she did not blame me because I told her quick."

He said his mother had to take him to the toilet at night.

"Why don't you go by yourself?"

"Because I am afraid."

The lad had been made to shamefully deny his normal anger and occasional intense hostility. This submerged emotional conflict was a cause of his misbehavior and unreasoning handicapping fears.

By means of play therapy with the family of dolls and a gorilla, he was able to discharge and act out his hostility to his younger, favored brother and to the others in the family. This resulted in the disappearance of his fears, which had been the reflection of his own disowned hostile feelings. During the play therapy he learned that the Witch represented his own "bad self." An account of the way in which this came about follows. The essential steps in the treatment are numbered and correspond to the numbers on Chart III.

Donald was shown a mother doll holding a baby doll in her arms. He was told, "A boy doll came to the door and saw them. What does the boy doll want to do?"

CHART III. RELATIONSHIP OF NEUROSES TO AGGRESSIVE BEHAVIOR

Neurotic Symptom Formation

Hostility → Repression → Fear Sensations (appear to come from arousing incident).

Resolution

Fear → Overcoming Guilt and Repression → Hostile Emotions Discharged.

Example

Donald, 6 years of age. Witch is projection of his own "bad" self.

Symptoms

Fear of dark, destructiveness, jealous, dreams "Witch stabs nose into me."

1. *Play* R—Boy overcomes rivalry guilt and pushes S doll off Mother's lap.
2. Guilt, fear, worry—"It made me mad too."
3. Mad at Witch.
4. Denies hostility to M, S, and F.
5. Releases it *by proxy*—has Witch eat F, M, and S dolls.
6. Punishes self by having Witch eat Boy Doll.
7. Reassurance given by no rebuke from therapist.
8. Identifies Self as Boy Doll.
9. Witch acts for him.
10. "I know"—Wants to keep Gorilla-Witch.
11. Releases hostility—Witch smashes baby S, M, and F dolls.
12. Verifies Boy Doll is Himself.
13. Asked who Witch represents?—"I don't know."
14. Made to feel O.K. to be bad (mad) sometimes.
15. Identifies Witch as Self.
16. More guilt dilution by doctor.
17. Again identifies Self as Witch—happier without guilt.
18. Later explains to M—"There aren't any Witches. It is just me when I'm a naughty boy" (laughs).
19. Symptoms disappear.

He replied, "The boy doll wanted the mother to love him."

"Show me."

He put the boy doll in the mother's arms and left the other child there also. A few minutes later he had the boy doll push the baby doll off the mother's lap.(1)

He was asked what he worried about and answered, "My fears. It made me mad too."(2)

"At whom do you get the maddest?"

"The Witch." (3)

"Others?"

"No one else."(4)

The doctor put the family of dolls to sleep on the toy beds, and the figure of a gorilla was used as a Witch. Donald was told, "Here's the Witch, what does she do?"

"She is going to eat up the babies."

"Show me!"

"Like this." (Donald had the Witch first "eat up" the father doll, next the mother doll, third the baby doll(5), and last the boy doll.(6)

No rebuke was given.(7)

He was asked, "Who is this?" (pointing at the boy doll).

"Me."(8)

"With whom is the Witch the most friendly?"

"This" (pointing to the boy doll).

Donald was queried, "So you really don't need to be afraid of the Witch if she is your friend and she ate the rest of the family first?"(9)

He answered, "Because I know." (10)

Donald then asked to keep the Witch, but was told it belonged to all the children who came to the office.

The doctor asked, "What does the Witch want to do?"

Donald then gave the Gorilla-Witch the rolling pin for a club and smashed the baby, mother, and father dolls. (11) While doing so he asked in a childish, disgruntled way for a game. He was told this was a game.

Seeking to verify and further develop the identity of the figures, some questions were repeated. "Whom did you say the Witch liked best?"

"The boy doll."

"You did tell me who the boy doll is?"

Donald's face brightened with a smile and he replied, "Me."(12)

He was again reminded, "Then you won't be afraid of the Witch because the Witch likes you more than the others. Who really is the Witch?"

"I don't know."(13)

He again asked for the Gorilla-Witch to take home.

The examiner said, "Who is this?" (pointing to the boy doll).

"Me."

"Is he a good boy sometimes?"

"Yes."

"Is he a bod boy sometimes?"(14)

"Yes" (manifest relief).

Again pointing to the boy doll, the doctor asked, "Who really is this?"

After a period of thought, Donald's face brightened and he said, "The Witch."(15) Then he again wanted to take the Gorilla-Witch home. This youngster seemed troubled.

He was asked if everyone did not get mad sometimes and replied in the affirmative.(16)

Donald was reassured that it was all right to get mad.(16)

"What did you learn here today?"

"Who the Witch is."(17)

Donald seemed brighter and more carefree.

A number of times after the interview, he wanted to come back and play some more of that game. The boy was encouraged to tell his mother what he had found out and later told her he had found out who the Witch was. The mother was advised not to question him further.

Donald's mother reported that the evening of the day of the above interview, the boy talked again of finding out about the Witch. Two nights later, when going to bed, Donald had looked under the bed. His mother asked for what he was looking. He had replied, "I am looking for the Witch," and laughed. He had added, "There aren't any Witches. It is just me when I am a naughty boy."(18)

Ten days later the mother phoned saying Donald was quite well-behaved, had no fears, and did not fight so much with his brother.(19)

After an interval of three months, a follow-up inquiry reported no recurrence of the fears, and satisfactory school and play adjustments. On a visit by the grandmother (formerly likened to the Witch), the boy had been friendly and shown none of his former disrespectful behavior. The mother recalled that the grandmother had, when Donald was little, read him many fairy tales. The grandmother's favorite had been about a bad witch.

Donald's mother said she had several times tried to stimulate in him a fear of witches, by reading him gruesome fairy tales about them, but he only laughed at them.

Ten months after the initial treatment, during a psychiatric re-examination, Donald stated his fears had evaporated after the play therapy, and that he had remained free of them. A social service follow-up after another five months revealed a continuing good adjustment.

This boy had disowned his own hostile feelings and they had been turned against himself. When he became conscious of these hidden feelings, discharged them in action and could accept them without so much shame, his fears passed away. Donald became better behaved and was not distracted by the emotional turmoil which had kept him from applying himself at school. The extreme jealousy of his younger brother disappeared. There was no more reason for him to be disrespectful to his grandmother, whom he had associated with the Witch.

This example shows what may be behind unacceptable neurotic behavior. It also illustrates, in a case of this type, the futility of excessive punishment and shaming, which only serve to increase the troublesome hostility and the causative unnecessary guilt feelings.

Donald's mother had been advised how to help her son control unacceptable aggressive impulses, without inducing shame and guilt. When the boy's behavior showed resentment, she could say, "Donald, I don't blame you for being mad when you can't do things; just learn to control it so others will like you." Thus she had recognized the naturalness of hostility and encouraged its control rather than the anxiety-producing repressive denial of its existence.

The prevention of emotional disorders lies in the management of the very young. Some very young children, who are raised strictly, shamed and never allowed to get dirty, become overly quiet, timid, and do not engage in active play. They may show minor fears, sleep disturbances, and the like.

Dr. David M. Levy has shown that, if these youngsters are given a few sessions of play therapy, during which they can be stimulated to play with clay, dirty themselves, or play out aggressive impulses, they soon show a normal spontaneity, aggression, and activity. From this, it can be seen that the *fundamental objective is to keep the natural human energies free for useful growth,* in the various phases of emotional character development. The relief of neurotic conditions releases energy previously blocked and makes such advances possible.

The cycles of aggression, guilt, and self-punishment are involved in normal growth during the adaption of the natural original self-interest to social living. With this information, it is easy to understand why neurotic attributes occur in all people. It is also interesting to note that these same cycles, in a more exaggerated form, are strikingly exhibited during the treatment of the emotionally sick child or adult.

Watch children as they grow and fit themselves gradually into society. Close observation reveals the following steps, which are repeated over and over again:

a. *A release of angry aggression* occurs in many forms, i.e., show of anger, striking movements, explosive speech, destructive acts, fighting, or more disguised forms as teasing, sarcasm, reproof, or other more refined ways of being mean.

b. Guilt feelings frequently arise after hostile expressions.

c. Next, *guilt-tinged self-punishment* may occur in some form, i.e., sulking, sobbing, unhappiness, refusal of dessert, self-reproof, apology, or seclusiveness, refusal to play, inviting punishment by misbehavior, "accidental" self-injury, etc.

d. After a time more aggression may be followed by guilt and by some form of retribution.

This *cycle continues* over and over again, *gradually becoming better controlled and less intense* (we hope) as socialization progresses. The adult forms of aggression become more disguised and less obvious. The hearty greeting with the painful slap on the back eloquently attests the mixed emotions present. The exclamation, "O dear! What a gorgeous dress you have on. Is it a new one? Mrs. Smith wore one exactly like it last night," is self-explanatory.

CONCLUSIONS

While there is a danger in oversimplification and in ignoring the other basic factors in the production of neuroses (such as faulty attitudes to sex, oedipal rivalries and emasculation fears), many parents can utilize certain basic concepts. Those emphasized here may be summarized as follows:

Hostile aggression is the natural outcome of the usual training restrictions, to which all children are subjected. The avoidance of inducing repression by means of excessive shame and guilt can prevent childhood misunderstandings, and can play *a part* in the prevention of neuroses. Say, "Johnny, I don't blame you for being mad. Just learn to control it! Then people can like you." Overtraining to be too good at too early an age is a great hazard. Allowing some aggressive, even hostile, behavior is safer than trying to stamp it all out. Simple control can be successfully taught, and adequate socialization thus acquired.

Comments on Current Literature

INFECTIOUS MONONUCLEOSIS

MENINGOENCEPHALITIS may result from the invasion of the nervous system by a variety of etiological agents, and on clinical grounds alone it is extremely difficult to establish a definitive diagnosis. In many cases viral etiology is suspected clinically, and where proper facilities are available, such clinical impressions can be verified in the laboratory by means of appropriate antibody studies and by isolation of virus from body fluids. In the November, 1950, issue of the *Annals of Internal Medicine*, Bernstein and Wolff[1] report that meningoencephalitic involvement of the central nervous system may occur in cases of infectious mononucleosis. These authors present a critical review of cases reported in the literature and add a case of their own. Using specific criteria, which were considered necessary for establishing the diagnosis of infectious mononucleosis and for establishing involvement of the nervous system, Bernstein and Wolff selected, as acceptable for analysis, thirty-four of the forty-six cases reported in the literature between 1931 and 1947.

An excellent summary of pertinent data collected from these cases reported in the literature is presented in their Table I; of the thirty-four selected cases, four had been classified as "serous meningitis," nine as "meningitis," four as "encephalitis," four as "meningoencephalitis," seven as "meningitis or meningoencephalitis with acute polyneuronitis," and six as "peripheral neuropathy." Perusal of this material re-emphasizes the oft-repeated statement that infectious mononucleosis is protean in its manifestations, and indicates clearly that involvement of the central nervous system is not infrequently associated with this clinical entity.

In reporting their own case, the authors review in considerable detail the studies carried out on a 19-year-old male patient who showed the usual manifestations of infectious mononucleosis, and who had, in addition as part of his clinical picture, definite findings of meningoencephalitis. Recovery was complete within thirty days. The authors state that "the entire clinical picture was indistinguishable from other forms of encephalitis."

It is significant to point out in the light of this report that the etiology of infectious mononucleosis has not been established definitely up to the present time. The virus theory has presented certain attractive features. Burnet and Anderson,[2] for example, have described the agglutination of human red cells sensitized by the virus of Newcastle disease with serum samples from patients with infectious mononucleosis. While virus etiology for this infection has not been established, patients having central nervous system involvement present clinical features which suggest strongly that a viral agent may be implicated. Pathologic studies are not numerous. However, the pathologic picture in excised lymph nodes has been described by a number of authors, and in 1947 Allen and Kellner[3] reported the autopsy findings on a patient with infectious mononucleosis who had met with accidental death. In referring to this report by Allen and Kellner, Bernstein and Wolff point out: "It is of extreme interest to note here that section of the brain showed that a few blood vessels in the cerebral cortex revealed a heavy cuffing of mononuclear cells, mostly lymphocytes, despite the fact that the patient did not have any symptoms of nervous system involvment."

The spinal fluid changes observed have consisted in pleocytosis, mainly an increase in lymphocytes, not described morphologically as "monocytoid" cells, and an increase in spinal fluid protein content. Sugar and chlorides are within normal limits and heterophile antibody has not been detected in the spinal fluid. It is of considerable interest that, as in the case of mumps, changes have been demonstrated in the cerebrospinal fluid of patients with infectious mononucleosis in whom there were no clinical signs of mental, motor, or sensory defects. Actually a comparison of nervous system involvment in infectious mononucleosis with that in mumps reveals many similarities. Since mumps is a known virus disease, such observations as these would tend to support the concept that the agent of infectious mononucleosis is viral in nature.

Infectious mononucleosis is predominantly a disease of children. Nevertheless, in their survey of the literature, Bernstein and Wolff encountered only one report of involvement of the nervous system in a child.[4] It is entirely possible, as has been demonstrated repeatedly in the case of mumps, that spinal fluid studies may reveal significant abnormalities in children without clinical manifestations of central nervous system involvement.

The authors suggest that heterophile antibody tests be done on all patients with "idiopathic" diseases of the nervous system since the clinical picture produced by involvement of the nervous system in infectious mononucleosis is indistinguishable from that brought about by other agents. Such investigations will prove of real interest and may serve to reduce further the number of cases of so-called "aseptic meningitis" and "meningoencephalitis," the etiological agent of which has not been established by the diagnostic procedures employed at the present time.

RUSSELL J. BLATTNER

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2. Burnet, F. M., and Anderson, S. G.: Modification of Human Red Cells by Virus Action: II. Agglutination of Modified Human Red Cells by Sera From Cases of Infectious Mononucleosis, Brit. J. Exper. Path. 27: 236, 1946.
3. Allen, Fred H., and Kellner, Aaron: Infectious Mononucleosis: An Autopsy Report, Am. J. Path. 23: 463, 1947.
4. Geliebter, Simcha: Infectious Mononucleosis Complicated by Encephalomyelitis, Lancet 2: 753, 1946.

News and Notes

Pediatric Calendar for 1951

American Board of Pediatrics:
Oral examinations: New Orleans, March 2 to 4.

American Academy of Pediatrics:
Area meeting: Cincinnati, March 26 to 28.
Annual meeting: Toronto, October 20 to 25.

American Pediatric Society:
Annual meeting: Atlantic City, May 3 to 5.

Society for Pediatric Research:
Annual meeting: Atlantic City, May 2 and 3.

American Medical Association:
Section on Pediatrics: Atlantic City, June 13 to 15.

Sir Leonard Parsons, who is well known by many American pediatricians, died suddenly of cerebral hemorrhage at his home in Birmingham, on Dec. 17, 1950.

Dr. Bertram R. Girdany, formerly of Babies Hospital in New York, has joined the Pediatric Staff of Children's Hospital of Pittsburgh in charge of the X-ray Department.

Dr. Clement A. Smith delivered the ninth annual series of the Benjamin Knox Rachford Lectureships Feb. 6 and 7, 1951, at the Children's Hospital Clinic and Research Building, Cincinnati, Ohio. The general topic of his lectures was "The Valley of the Shadow of Birth."

Plans for an international cooperative study of the effectiveness of ACTH and cortisone in the treatment of rheumatic fever and the prevention of rheumatic heart disease have been developed and announced by the American Heart Association. Patients treated during acute attacks of rheumatic fever during 1951 will be followed for at least three years. There will be twelve cooperating research centers: New York City (two), Boston, Chicago, Denver, the Air Force Base at Fort Warren, Wyoming, Toronto, Canada, and at Newcastle, London, Taplow, Cardiff, and Sheffield in England. A grant of $200,000 has been made for the study by the National Heart Institute of the U.S.P.H.S., and Armour & Company and Merck & Company will contribute the ACTH and cortisone for the study. The investigation will be coordinated at the central office of the Association in New York.

As of Jan. 1, 1951, the American Board of Pediatrics has issued 3,466 certificates. Of this group, 152 are known to be deceased.

A five-day review in Pediatrics will be given by the Tulane University School of Medicine of New Orleans Feb. 12 through 16, 1951. The mornings will be spent in clinics and ward rounds, and afternoons demonstrations will be given in the basic science laboratories. The theme to be stressed in the course will be "The Contributions of Basic Science to the Practice of Pediatrics."

Pediatric Post-Graduate Course, Harvard Medical School, at the Burnham Memorial Hospital for Children, Massachusetts General Hospital, Boston, under the direction of Allan M. Butler, Professor of Pediatrics, June 11 through June 23 daily, 9 A.M. to 4:30 P.M. A broad review of pediatrics emphasizing the newer advances in diagnoses and therapy. For further information, write Courses for Graduates, Harvard Medical School, 25 Shattuck St., Boston.

A Fellowship in Pediatric Neurology is available in the Children's Division of the Cook County Hospital. For information concerning this appointment, write to Dr. Abraham Levinson, Chief of Staff, Cook County Children's Hospital, Chicago 12, Ill.

The following were certified by the **American Board of Pediatrics** at the examination at Boston, Mass., Dec. 1, 2, and 3, 1950.

Dr. Hyman Alford, 1755 Beacon St., Brookline, Mass.

Dr. Lewis A. Barness, Warrington, Bucks County, Pa.

Dr. William Randal Bell, 36 Locust St., Marblehead, Mass.

Dr. Thomas Berry Brazelton, 51 Brattle St., Cambridge 38, Mass.

Dr. William M. Browning, 3740 Central Ave., Indianapolis 5, Ind.

Dr. Joseph R. Christian, 414 S. Oak Park Ave., Oak Park, Ill.

Dr. Gene Hofmeister Clarke, 2300 Main St., Buffalo 14, N. Y.

Dr. Charles Davenport Cook, 121-A Brattle St., Cambridge, Mass.

Dr. John J. Drucker, 75 Ascan Ave., Forest Hills, N. Y.

Dr. Eileen Lanning Edelberg, Hopmeadow St., Simsbury, Conn.

Dr. Paul G. Eglick, 7342 Walnut Lane, Philadelphia, Pa.

Dr. Edmund Noyes Ervin, 33 College Avenue, Waterville, Maine.

Dr. John Gerard Flynn, 377 Essex St., Salem, Mass.

Dr. Francis H. Fox, 83 West St., Portland 4, Maine.

Dr. Bennett Lewis Gemson, 133 Rose Lane, New Hyde Park, L. I., N. Y.

Dr. Philip Given Good, 38 Deering St., Portland, Maine.

Dr. Leo F. Gowen, 549 Locust Court, St. Louis 19, Mo.

Dr. Sumner Hagler, 20 Bishop Rd., Quincy, Mass.

Dr. Albert E. Hensel, Jr., 1717 White St., Alexandria, La.

Dr. Harry Eugene Hile, Medical Arts Bldg., 3700 Fifth Ave., Pittsburgh, Pa.

Dr. John Platt Hubbell, Jr., 1101 Beacon St., Brookline, Mass.

Dr. John S. Hyde, 1102 N. Harlem Ave., River Forest, Ill.

Dr. David Mifflin Jones, 1406 S. 18th St., Lafayette, Ind.

Dr. Stuart Lorin Joslin, 27 Unquowa Rd., Fairfield, Conn.

Dr. Hans George Keitel, Massachusetts General Hospital, Boston, Mass.

Dr. Anna Katharine Kiehl, 639 Washington St., E. Walpole, Mass.

Dr. Barbara Maria Korsch, 26 Bank St., New York 14, N. Y.

Dr. Robert Lathrop Landgraf, 107 N. Second St., Niles, Mich.

Dr. Robert D. London, 28 E. 73rd St., New York, N. Y.

Dr. Alexander S. MacDonald, Jr., 1 Monument Square, Beverly, Mass.

Dr. Paul F. Maness, 305 West Front St., Burlington, N. C.

Dr. Robert James McKay, Jr., Mary Fletcher Hospital, Burlington, Vt.

Dr. Russell Auger Morisette, 70 Pine St., Lewiston, Me.

Dr. Edna Zeltner Mortimer, 1409 West Acres Rd., Joliet, Ill.

Dr. Cornelius H. Nau, 647 Moore Bldg., San Antonio 5, Tex.

Dr. Robert J. Norton, 194 Arlington Ave., Brooklyn 13, N. Y.

Dr. Michael Orange, 601 East 19th St., Brooklyn, N. Y.

Dr. William David Penhale, 1 South St., Concord, N. H.

Dr. Harold Perkel, 441 Boulevard, Bayonne, N. J.

Dr. M. Edwin Pesnel, 540 New Scotland Ave., Albany, N. Y.

Dr. William Peter Riley, 86-07 96th St., Woodhaven, N. Y.

Dr. Albert Philip Rosen, 3-16 Kenneth Ave., Fair Lawn, N. J.

Dr. Alvin J. Schneider, 1155 10th Avenue, North, Seattle 2, Wash.

Dr. William C. Smith, 525 West Main St., Waynesboro, Va.

Dr. Gustav G. Steneck, 275 River Rd., Bogota, N. J.

Dr. John Wily Garrett Tuthill, 510 Boston Post Rd., Weston 93, Mass.

Dr. Charles Orlan Tyler, Grove St. and Rhoads Ave., Haddonfield, N. J.

Dr. George Robert Wade, 129 Chester Ave., Moorestown, N. J.

Dr. John Knox Wilson, 1012 North Elm St., Greensboro, N. C.

Dr. Paul Wilson, 175 E. 79th St., New York 21, N. Y.

Dr. Robert F. Wilson, 113 Locust St., Dover, N. H.

Dr. I. Robert Wood, 71 Court St., Plattsburg, N. Y.

Book Reviews

An Atlas of Human Anatomy. Barry J. Anson, Ph.D., Philadelphia, 1950, W. B. Saunders Company, 518 pages. Price $11.50.

This *Atlas of Human Anatomy* by the professor of anatomy at Northwestern University Medical School is a valuable addition to the texts for the medical student and for the physician who wishes to refresh himself on some anatomic point or question. Many of Professor Anson's graduate students who were working on research problems have contributed. Great praise must be given to the group of medical illustrators who were responsible for the drawings made from the preparations. As the author states, the success of such an atlas depends largely on the skill of the illustrator, and in this volume the drawings are distinctly superior. The inclusion of considerable material on what might be termed normal variations is of particular value in keeping with the developments of modern surgery. The printing is excellent and the details of the drawings stand out clearly and sharply.

Pathologic Physiology: Mechanisms of Disease. Edited by William A. Sodeman, M.D., Philadelphia, 1950, W. B. Saunders Company, 808 pages. Price $11.50.

Nothing could more graphically reflect the changes which have been taking place in the clinical departments of the medical schools than this text on pathologic physiology. Nearly all of the twenty-five contributors to the text, which is edited by Dr. Sodeman of Tulane, are from departments of internal medicine, and are primarily clinicians. It is questionable if a similar text would have been possible twenty years ago. Instead of the usual approach of a medical text, disease is presented from the standpoint of physiologic dysfunction, analyzing the mechanisms of the various signs and symptoms as they are seen in the patient. The text considers the subject by systems starting with the circulatory, followed in turn by the respiratory, digestive, and so on. From its very nature the text cannot be reviewed in detail, but the clinician will find assembled in it a mass of information that he otherwise would have to search out through a multitude of books and medical journals. As a rule, the technical details are presented in a readable and understandable form. The book clearly reflects the vast strides that have been made in elucidating the mechanisms of disease. It is one of the most important medical texts that has appeared in years, as it brings together our knowledge of the mechanisms of disease.

Teaching the Retarded Child at Home. Edna Davison Osterhout, B.A., Durham, 1950, Duke University Press. Price $2.25.

Among the problems which the pediatrician has to meet is the difficult one of advising parents of a retarded child. His advice will be influenced by many factors, as the degree of retardation, the economic status of the family, the question of siblings, the accessibility of special schools, and the like. One thing that he must always stress is the importance of working to bring out to the fullest the potential capabilities of the infant or child. This implies hard, patient work on the part of the parents and specific advice on what to do. This little handbook on *Teaching the Retarded Child at Home* will be of great help to the parents and caretakers of a retarded child in the home when for some reason or another a special school is not possible. It is based on practical, proved experience in the teaching of retarded children. It serves as a guide for preparing the material needed in teaching for a "beginner teacher." The rate of progress of a retarded child will, of course, be dependent on the degree of retardation and the patience and zeal of the teacher. The interest and encouragement of the medical adviser is of utmost importance. It is material which the pediatrician should know is available and can be recommended to parents faced with the training and education of a mentally backward child.

Microphthalmos and Anophthalmos With or Without Coincident Oligophrenia. A Clinical and Genetic-Statistical Study. Torsten Sjögren and Tage Larsson, Copenhagen, 1949, Ejnar Munksgaard.

This is an interesting Swedish study of 137 cases of microphthalmos with (Mo) and without (Mi) coincident oligophrenia. Fifty-five of the cases were of the combined (Mo) type which was described in 1922 by Ash in Great Britain. Each of the conditions represents 4 per cent of the blind children of school age in Sweden. Such questions as familial and geographic distribution were carefully studied. The authors conclude that Mo cases may be a partially sex-linked inheritance, and that Mi occurs as a dominant hereditary disease to a certain extent. It was not possible to determine the extent caused by exogenous factors. The monograph will be of particular value to those interested in the genetic factors in etiology, and the authors are to be commended for the painstaking care with which the study was conducted.

Nutrition in Health and Disease. L. F. Cooper, E. M. Barber, H. S. Mitchell, and H. J. Rynbergen, ed. 11, Philadelphia, 1950, J. B. Lippincott Company, 744 pages. Price $4.00.

The new eleventh edition of this well-known text by four nutritionists and dietitians has been extensively revised since last published in 1947. Part one deals with the principles of nutrition, and the dietary charts have been revised. Part two on diet in disease includes recent advances in diet for hypertension and cardiac disease. Part three is on food selection and preparation. Part four, containing tabular material, has been brought up to date.

A Manual of Cerebral Palsy Equipment. Chicago, 1950, National Society for Crippled Children and Adults, Inc.

This is an excellent manual of 127 different types of equipment for the use of the child with cerebral palsy. Material in use in many centers has been collected. Each article is described and shows a photograph of its actual use. A large-sized working drawing is furnished for each article which makes local construction possible. The preparation of the manual was aided by a grant from the Zeta Tau Alpha national fraternity for women.

Die Erkrankungen der endokrinen Drüsen. (Diseases of the Endocrine Glands). Adolph Oswald, M.D., Bern, 1949, Medizinischer Verlag Hans Huber, 580 pages. Price 58.00 Swiss francs.

There are many excellent textbooks available in the field of endocrinology. The difficulty with most of them is that they are too voluminous for everyday use, and that they all become so easily obsolete with the rapid advancement of medical science.

This book by Dr. Oswald makes a valiant, and on the whole rather successful, attempt to meet both of these objections, as far as it is possible in a textbook of this kind.

It is not overwhelmingly large, and it still succeeds in covering the entire field of endocrinology. The division of the subject matter follows the accepted line, i.e., according to the physiologic systems.

The general introductory chapter gives the reader a concise and clear bird's-eye view of our basic knowledge of the endocrine systems. Physiology of the hormones, the neuroglandular system, the interdependence of the endocrine organs, the relationship of endocrine functions with the vitamins, the role of the hormone apparatus in defense functions, the influence of the neuroendocrine set-up upon the psyche—these are all very satisfactorily covered. General pathology and therapy round out this chapter. In the special chapters the same pattern of presentation is followed. Anatomy of the glands, their physiologic functions, biochemistry, disorders of secretions and their significance for the other systems, and the organism as a whole are everywhere discussed in a clear and well-balanced manner.

Related literature is covered as completely as it is possible in a book of this size. American authors are widely and frequently quoted on almost every page.

The style of Oswald is easy and not at all as involved as German texts are so often likely to be.

The book may be suggested with confidence to American readers who command the German language. ZENTAY.

Editor's Column

THE NUMBER AND DISTRIBUTION OF PEDIATRICIANS

IN A recent discussion the question arose as to the number of pediatricians now in practice, and the number that might be expected by the mid-fifties. While there is no way in which definite figures can be obtained, some estimates are possible. As a basis a start may be made with the Survey study, which gave a figure of 3,507, compiled mostly in 1946. In the three years 1948, 1949, and 1950, the Board certified 764 pediatricians in the United States. This figure includes some who were included in the Survey report, and deaths have occurred. In addition, a number who failed the examination and others who did not take the examination are in practice. An estimate of the group in the interval between the two compilations may be put at 200 certified and 100 for the noncertified group. As of Jan. 1, 1951, the Board reports over 450 who will have finished their five-year period of training and are eligible for examination in 1951. Further, a large group finished hospital residencies in 1949 and 1950 and are now in their two-year period of practice before becoming eligible for examination. These combine as follows:

Survey Report	3,507
Interval	200
Certified 1948, 1949, 1950	764
Noncertified	100
Ready for certification 1951	450
Completed residency	750

In this way an estimate is reached, which is somewhere close to the actual figure and on the conservative side, that as of Jan. 1, 1951, there are approximately 5,700 pediatricians in the United States. Of these, over 5,000 are busy in the unique American development of pediatric private practice.

Our approximate 1,000 pediatric hospital residencies have been filled in the last three years and some 400-odd are completing this part of their training each year. How much present world conditions will interfere with their training and entering practice is in the lap of the gods. Granted too much interference does not develop, there should be another 1,500 added by 1956. This would make a total of over 7,000 pediatricians, which would be an increase of 3,500 or 100 per cent in the ten-year period following the Survey study. Certainly, pediatrics as a specialized field of medical practice is growing by leaps and bounds.

DISTRIBUTION

The Survey report presented a map (Fig. 23, p. 37) showing the distribution by states and regions of the 3,507 pediatricians. The question is of interest as to whether the same pattern of distribution is holding for the men who have entered pediatrics since 1946. The only available figures for comparison are those certified in recent years. While the number is undoubtedly larger, and a few are included in both groups, the certified group is sufficiently large to indicate trends.

At seventeen examinations, December, 1947, through December, 1950, 816 were certified by the Board of Pediatrics, including nine from outside the states. We thus have the distribution of 807 to compare with the Survey report. The seventeen examinations were widely distributed. Seven were along

Survey Report				Certified in 1948, 1949, 1950	
Region	% of child population	Pediatricians			
		No.	%	No.	%
Northeast and Central	43	2,144	61.1	464	57.5
Pacific	8	407	11.6	108	13.4
Mountain and Plains	12	260	7.4	86	10.8
Southeast	28	501	14.3	108	13.3
Southwest	9	195	5.5	41	5.0
	100	3,507	99.9	807	100
New York, Pennsylvania and Massachusetts		1,116	31.8	240	29.8

the Atlantic seaboard from Boston to Richmond, seven in the Middle West, two on the Pacific coast, and one in the South. While there is a preponderance of regional candidates at examinations, usually many different states are represented. Thus the thirty-eight certified in St. Louis in 1949 represented nineteen states. At Cincinnati in 1950, the fifty-two certified came from twenty-seven states. With seventeen widely distributed examinations, the total figure is not influenced much by the place of examination.

The Survey report divided the country into five regions, and the 807 certifications have been placed into the same grouping for purposes of comparison.

It is thus seen that there has been no marked change in distribution when a division is made into regions. There is a small decrease in the Northeast and Central (3.6 per cent), and small gains in the Pacific, and Mountain and Plains regions. Every state in the Union is represented in the 807, which is 23 per cent of the number reported in the Survey report. Five states had a gain of only one. The increase in New York, Pennsylvania, Illinois, Michigan, Connecticut, and Texas was close to the 23 per cent figure. California showed a gain of 25 per cent, Massachusetts 27, Missouri 28, and New Jersey 29. Some of the states with a percentage gain below 23 were Georgia 6.6, Arizona 8, Vermont 9, Arkansas 11, and New Mexico 14 per cent. Some states with few pediatricians in the Survey report had a large gain percentagewise. Thus North Dakota increased from six to ten, or 66 per cent. Wyoming added one to one, or 100 per cent. All in all no marked change by states or regions seemingly has taken place in the last five years.

There has been an impression of an increasing trend for pediatricians to locate and practice in the smaller cities. The Survey report states (p. 37) that 75 per cent of the pediatricians were located in cities of 50,000 or more.

A comparison of 215 certified in 1947 was made with the last 216 certified in 1950. The suburbs of the large metropolitan areas were included in the Metropolitan groups.

	1947		1950	
Metropolitan areas	95	72%	78	57%
Large cities	60		45	
Small cities	60		93	
	215		216	

Thus there is seemingly a distinct trend for the recently certified pediatricians to locate in the smaller cities, even if there is little change in the distribution by regions and states.